LIBRARY
BOSTON UNIVERSITY
SCHOOL OF MEDICINE

The Journal of
Thoracic Surgery

VOL. 16 FEBRUARY, 1947 No. 1

Original Communications

SURGICAL THORACIC TUMORS IN NAVY PERSONNEL

WILLIAM LAW WATSON, M.D., F.A.C.S., NEW YORK, N. Y., AND
LIEUTENANT HENRY D. DIAMOND, MEDICAL CORPS, UNITED STATES
NAVAL RESERVE (BY INVITATION)

THE United States Navy for a number of years has provided specialized medical care for its patients suffering from cancer and allied diseases. In keeping with this modern and farsighted policy, the following measures are taken to insure each patient with suspected or proved neoplastic disease prompt and adequate medical and surgical care.

First, and of foremost importance, the Naval Hospital at Brooklyn, N. Y., is designated as the regular treatment hospital for neoplastic cases in the Navy, to serve ships and stations on the Atlantic Coast and in the Ninth Naval District.

Second, every patient suspected of harboring a neoplasm is seen in consultation with a member of the attending staff of Memorial Hospital, and treatment is outlined and carried out under the direct supervision of the chief of service.

Third, an adequate supply of Government-owned radium is on deposit at Memorial Hospital for use in the treatment of Navy patients, and two beds are set aside for the exclusive use of these patients when special surgical care is needed. This provision makes it possible to take advantage of the services of a thoracic surgical team for the care of naval personnel during times of peace, as it was done during the war.

Fourth, several of the younger medical officers in the regular Navy have been given fellowship training at Memorial hospital, and these men have then been placed in charge of the tumor service of the Naval Hospital at Brooklyn, thus providing skilled medical follow-up care.

As was anticipated, the incidence of tumor cases admitted to the hospital began to show a definite increase coincident with the rapid expansion of naval manpower following Pearl Harbor. The increase was steady and reached its

Read at the Twenty-Sixth Annual Meeting of The American Association for Thoracic Surgery, Detroit, Mich., May 29, 30, and 31, 1946.

peak late in the Fall of 1945, when the tumor service had increased fivefold and the daily census of hospital cases of neoplastic disease was running about 160. To aid in the care of these patients, the Navy commissioned three members of the attending staff of Memorial Hospital.

MATERIAL

The material for this report has been selected from among the patients studied and operated upon during a three-year tour of duty at the Brooklyn Naval Hospital. In that period some 746 cases of neoplastic disease were seen and treated. Of this group, there were thirty-three patients with intrathoracic tumors suitable for surgery. Due to the exigencies of war and the urgent necessity of returning every available man to duty as soon as possible, operations were avoided whenever practicable.

Patients with such diseases as primary mediastinal Hodgkin's disease, malignant thymoma, Boeck's sarcoid, and hilar tuberculosis are not included in this report, nor would anything be gained by discussing at this time the cases of inoperable cancer of the lung and esophagus.

Of the thirty-three thoracic tumors in this series considered suitable for surgery, twenty-four were found to be benign, and nine malignant. In relation to the total number of cases of neoplastic disease admitted for treatment, surgical thoracic tumors occurred in the ratio of 1:23, and malignant tumors in the ratio of 1:83.

AGE AND SEX

As one would suspect, the age of our patients was much less on the average than is found in civilian practice. The youngest patient in this series was 17 years of age and had a bronchogenic cyst. The oldest was 47 years old and had a bronchogenic carcinoma. The average age of all patients was 28 years. The youngest patients with malignant disease were two enlisted men, each 21 years of age, with malignant chest wall tumors, one a Ewing's tumor and the other a malignant endothelioma. All the patients were males. There were a number of Waves admitted as patients on the tumor service, but no thoracic tumor was discovered among them.

SYMPTOMATOLOGY

The usual clinical symptoms which lead to the making of a definite diagnosis of intrathoracic tumor need no emphasis. In the series of cases under consideration, there were, however, twenty-three instances in which the patient's tumor was discovered before it had caused any symptoms worthy of note, or had inconvenienced him enough to warrant his reporting for investigation. Of these asymptomatic tumors, eighteen proved to be benign, and five proved to be highly malignant.

TREATMENT

In thirty cases in which data are complete, there were ten instances of excision of a mediastinal tumor, nine exploratory thoracotomies, four total pneumonectomies, and four partial pneumonectomies or lobectomies. Three thoracic

TABLE I. SURGICAL THORACIC TUMORS IN NAVY PERSONNEL

PART AFFECTED AND TYPE TUMOR	NO. CASES
Lung:	
Cancer	3
Bronchogenic cyst	3
Bronchial adenoma	2
Mesothelial sarcoma	2
Tuberculoma	1
Pheochromocytoma	1
Inflammatory lesions	5
Chest Wall:	
Osteochondroma	1
Endothelioma of pleura	1
Ewing's tumor	1
Mediastinum:	
Lymphoma	2
Aneurysm	2
Schwannoma	2
Cystic hygroma	1
Calcified dermoid	1
Ganglioneuroma	1
Hemangioma	1
Malignant tumor	3

wall tumors were resected; two of these were very malignant, and one was benign. In two instances, the thoracic wall defects were large and were repaired by free grafts of wide sheets of fascia lata. The following is a discussion of the most interesting cases.

CASE REPORTS

CASE 1.—J. B., 29 years of age, had a chief complaint of repeated attacks of left chest pain accompanied by fever, a productive cough, and occasional hemoptysis. A positive bronchoscopic diagnosis of adenoma of the left main stem bronchus was established. Repeated, partial bronchoscopic removal of tumor and treatment with large doses of penicillin resulted in marked clinical improvement, cessation of all symptoms, and a gain of 22 lbs. in weight. He was given a two-week leave from which he returned abruptly due to a high fever, cough, and chest pain. Radiographs revealed a typical complete left-sided atelectasis.

Operation.—Left total pneumonectomy was done through a posterolateral approach. The lung was found to be densely adherent to the parietal pleura with numerous adhesions binding it to the mediastinum. Individual ligation of the hilar structures was carried out with some difficulty. The operative specimen was a well-fixed, rounded, somewhat pedunculated tumor mass measuring 1.5 cm., and completely obstructing the first portion of the main bronchus.

Microscopic Examination.—The tumor was composed of variable sized, polyhedral-shaped, epithelial cells with both clear and dense cytoplasm. The nuclei stained deeply and varied greatly in size. Mitotic figures were common. The tumor did not invade structures adjacent to its original site. An adenomatoid structure was suggested.

Histologic Diagnosis.—The histologic diagnosis in this case is not entirely certain. Our pathologist prefers to call this tumor a pheochromocytoma, a tumor of kidney origin characterized by chromaffin cells which secrete epinephrin. Other pathologists have called it a malignant bronchogenic adenoma. Clinically, I would call it a typical benign adenoma of the bronchus.

CASE 2.—H. D., 38 years old, had no complaints, but a lesion in the left lung was discovered on routine chest film prior to promotion. He was put on a limited duty status and

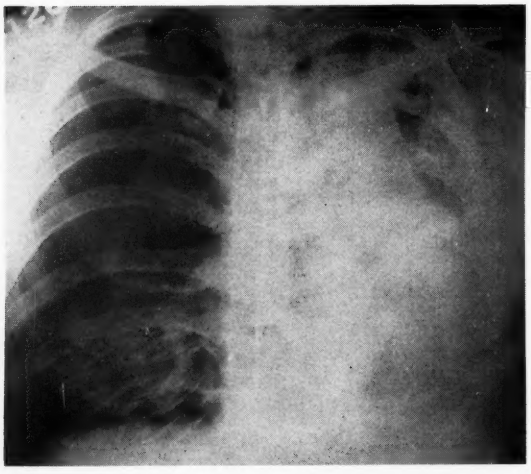

Fig. 1.—J. B. Radiograph of chest showing almost complete left lung atelectasis, deviation of the trachea to the left of the midline, and retraction of the heart and mediastinum to the affected side.

Fig. 2.—J. B. Operative specimen demonstrated that only a small portion of the apex of the lung remained aerated. At 1.5 cm. distal to the line of resection of the main bronchus, there was a smooth, reddish, granular, rounded, somewhat pedunculated, firm tumor mass 1.5 cm. in diameter, which was causing almost complete bronchial obstruction.

observed for eighteen months. During that time, he lost 25 lb. and became nervous and apprehensive about his condition. Physical examination revealed no abnormalities.

Operation.—Left posterolateral approach was used. A round, rubbery, yellowish-gray, well-encapsulated mass 5 cm. in diameter was found just beneath the visceral pleura in the periphery of the left lower lobe. A wide, wedge-shaped excision was done.

Gross and microscopic studies of the operative specimen revealed this lesion to be a typical tuberculoma.

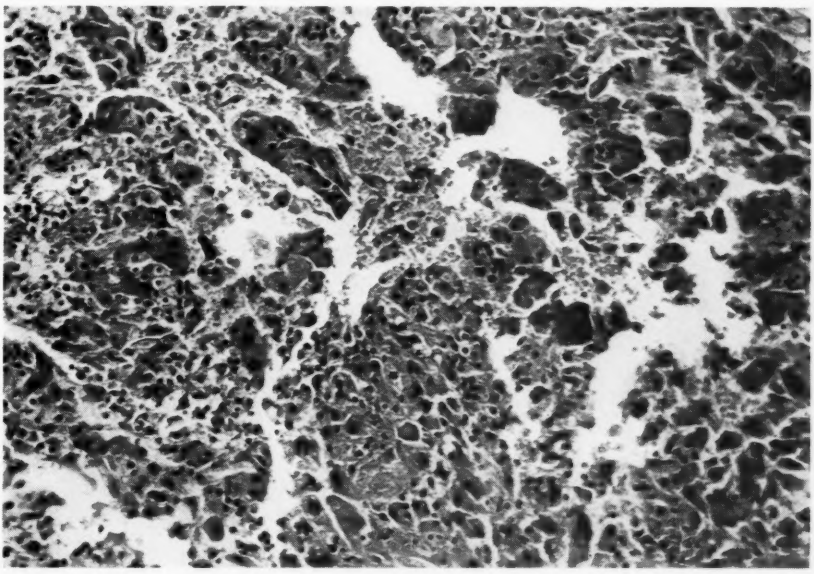

Fig. 3.—J. B. Microscopic study of the tumor revealed it to be composed of variable sized polyhedral-shaped epithelial cells with both clear and dense cytoplasm. The nuclei stain deeply and vary greatly in size. Mitotic figures are common. The tumor does not invade structures adjacent to its original site. An adenomatoid structure is suggested. Histologic diagnosis (opinion of competent pathologists is divided): (1) pheochromocytoma, (2) malignant bronchogenic adenoma, and (3) benign bronchogenic adenoma.

CASE 3.—H. H., age 25, also had no chief complaint. A routine chest x-ray revealed a mass 19 × 12 cm. in the left chest. This mass was thought by the roentgenologist and medical consultants to be a lymphomatous tumor, probably Hodgkin's in type, and x-ray therapy was given. The patient received 1,800 r through each of two portals 20 × 20 cm. in size. Five months after treatment, there was no change in the size of the tumor.

Operation.—A left anterior approach through the bed of the resected fourth rib was used. The tumor was of good size, and was compressing and densely adherent to the lung. It had to be separated by sharp dissection inferiorly and posteriorly from the pericardium and aortic root and arch, and superiorly from the left common carotid artery. The recurrent laryngeal nerve was severed at this point. A routine silk closure without drainage was done. An encapsulated mass, the shape of a smoked ham, measuring 19 cm. in length, 5 cm. in width above and 11 cm. below, and being nearly equal in thickness, was found. Consistency varied from firmness to soft fluctuation, and the color varied from deep purple to pale, yellowish gray.

Microscopic Examination.—Microscopic examination revealed thick-walled blood vessels, central hemorrhage and necrosis, a reticular disposition of the cell nuclei with many stellate forms, and one area of nerve tissue, leading to a diagnosis of necrotic Schwannoma. Other pathologists have called this an angiofibroma.

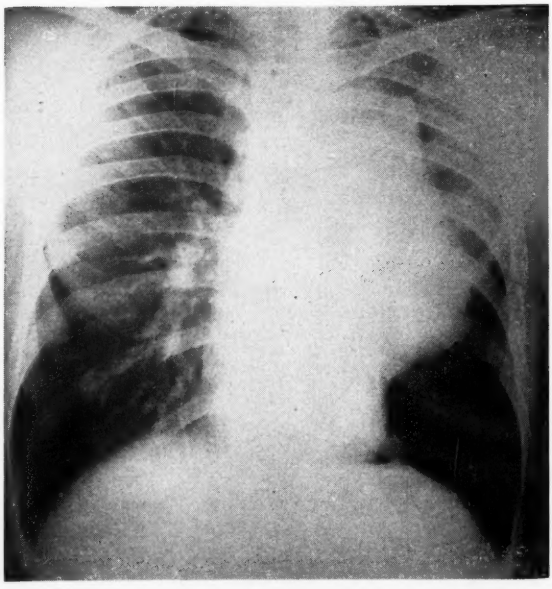

Fig. 4.—H. H. Routine chest radiograph revealed a large, lobulated mass measuring 19 × 6 cm., extending from the mediastinum out into the left chest. Lateral views showed the mass to extend posteriorly beneath the arch of aorta and also into the superior mediastinum. A radiographic diagnosis of malignant mediastinal lymphoma was suggested.

Fig. 5.—H. H. Gross specimen was a densely encapsulated, ham-shaped mass measuring 19 × 11 × 6 cm. Its consistency varied from rubbery firmness to soft fluctuation. On the cut surface the color varied from pale yellowish gray to deep purple. There were frank areas of old hemorrhage and some necrosis (probably radiation effect).

CASE 4.—G. K., aged 27, had no symptoms. A routine physical check-up and x-ray of the chest revealed an opaque mass in the left apex. Induction x-ray was traced and located and showed the same sized tumor in the left apex. Aspiration biopsy revealed tumor cells thought to be benign. Physical examination revealed no abnormalities.

Operation.—A posterolateral incision was made and the chest was opened through the bed of the partially resected fifth rib. A firm tumor mass in the apex was covered by thick, edematous, chronically inflamed, parietal pleura, which hung down in folds. The pleura was partly excised and frozen sections were done. The tumor was then excised. It lay in a bed bounded posteriorly by the second, third, and fourth dorsal vertebrae, and laterally by the curve of the second, third, and fourth ribs.

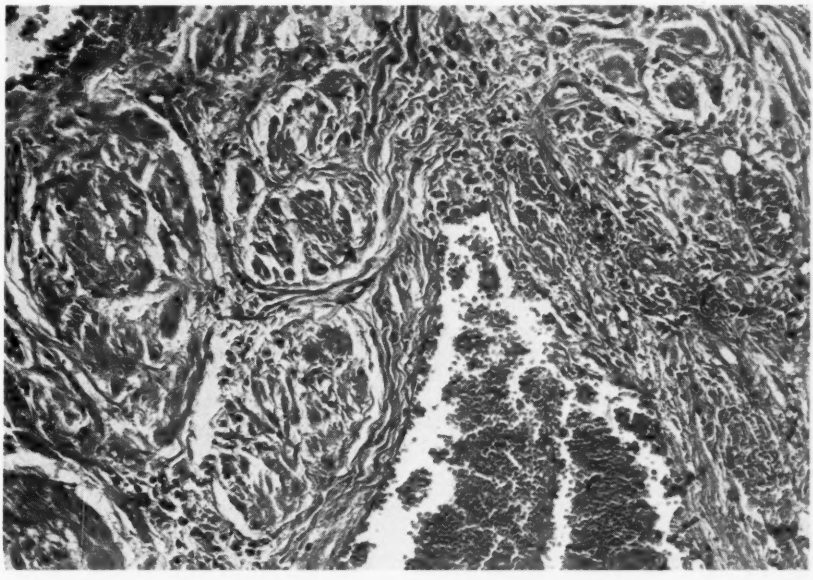

Fig. 6.—H. H. Microscopic study showed the tumor to be composed of concentric nodules of dense hyaline tissue and an adjacent dilated sinusoidal vessel, structural traits sometimes found in portions of necrotic Schwannoma. Histologic diagnosis (opinion of competent pathologists differ): (1) necrotic Schwannoma, (2) angiofibroma.

Microscopic Diagnosis.—The tumor was diagnosed as benign lymphoma, showing a diffuse overgrowth of typical small lymphocytes. There is some suggestive evidence regarding this tumor which leads us to view its benignity with suspicion, and prompts us to keep such patients under close observation for a long period of time. Simple lymphoma may be distinguished from leucemia by the blood test, and from pseudoleucemia by its local character, but from neither on the histologic structure alone. In the absence of the usual signs of malignancy, lymphosarcoma may be ruled out.

CASE 5.—S. P., aged 47, had a routine chest plate taken prior to transfer to the regular Navy which revealed an abnormal heart shadow. At this point, he first began to notice dyspnea on exertion, and found that he could sleep with comfort only when lying on his stomach, face down. Physical examination revealed slight cyanosis of the lips and finger tips. Electrocardiographic findings corroborated a physical diagnosis of mild mitral stenosis. An unexplained paralysis of the left side of the larynx was noted. Angiocardiograms showed that the tumor was nonvascular in origin.

Operation.—An anterior approach was made through the bed of the resected third rib. A hard, partly calcified, well-encapsulated mass 8 × 6 × 4 cm. was found springing from a broad mediastinal pedicle, and lying on the anterior surface of the left ventricle. It was excised without difficulty. Grossly, the tumor appeared to be a mediastinal dermoid. Histologically, all sections revealed that the epithelial wall had been lost and was replaced by a shell of bone. The contents were unidentifiable.

CASE 6.—P. F., aged 22, had no presenting symptoms. A chest x-ray during processing for discharge from the Marine Corps revealed a smooth, rounded mass in the left hilar region which transmitted pulsations. An enlarged node in the left axilla was excised and showed only chronic lymphadenitis. Tissue removed from the hilar mass by aspiration biopsy revealed large numbers of small and large nucleated cells resembling lymphocytes suggesting the diagnosis of lymphoma.

Operation.—A left anterior approach through the bed of the resected fourth rib revealed the tumor in the hilus extending outward in the interlobar fissure. The base of the mass was so adherent to the pulmonary artery that it was deemed wise to cut across the mass at this point, and submit the tumor to the pathologist for frozen section. When he reported the mass to be benign, no further excision was done.

Microscopic Diagnosis.—Benign, giant, follicular lymphoma. Clinically, some suspicion is attached to this particular brand of tumor.

CASE 7.—R. B., aged 30, was asymptomatic. A mass in the right lung was discovered on x-ray examination at a separation center March 4, 1946. Bronchoscopy March 21, 1946, and biopsy from the right upper lobe orifice showed squamous cell carcinoma, grade 2. Physical examination was normal.

Operation.—Operation revealed a large tumor of the right upper lobe invading the chest wall and extending into the upper hilar structures causing extensive induration and fixation. Several large metastatic nodes were in the peritracheal region.

Histologic Diagnosis.—Epidermoid carcinoma, grade 3.

Comment.—Bronchogenic cancer in the young is probably a very insidious and virulent disease. In this case, a patient with symptomless cancer of the lung had his tumor discovered by accident, and was given prompt surgical aid, and yet his tumor had already progressed beyond the stage of operative cure.

CASE 8.—F. S., aged 37, had a routine separation center chest radiograph taken, which showed a 5 cm., circumscribed area of infiltration near the left hilum. He then admitted having had a chronic, nonproductive cough for the preceding six months. There was no pain, night sweats, or loss of weight. Bronchoscopy revealed a polypoid mass in the left main-stem bronchus, and a biopsy was reported as squamous carcinoma, grade 2.

Operation.—Left posterolateral approach was used. The lung was densely adherent to the descending aorta, but the hilar structures were free, and no nodes were involved. A complete pneumonectomy was done, with individual ligation of the hilar structures. The tumor was located in the left main-stem bronchus about 2 cm. beyond the site of amputation. It sprang from the lateral wall through which it had extended to infiltrate the adjacent lung parenchyma.

The microscopic diagnosis was squamous carcinoma.

CASE 9.—P. H. F., aged 40, complained of occasional nonexertional dyspnea and left chest pain. This patient, a periodic drinker on neuropsychiatric consultation, was deemed unfit for useful service in the Navy. Chest x-ray revealed a small, decrete, rounded area of increased density in the left upper lobe. Aspiration biopsy was done and was reported as showing a malignant tumor, probably sarcoma. An intensive and minute examination was made for other evidences of malignant disease, or a primary source of disease, and none was found.

Operation.—The chest was opened through a left lateral approach. There were no adhesions or enlarged hilar nodes, and the only important finding was a rounded, hard, 5 cm. mass in the left upper lobe just beneath the pleura. A total pneumonectomy was done with

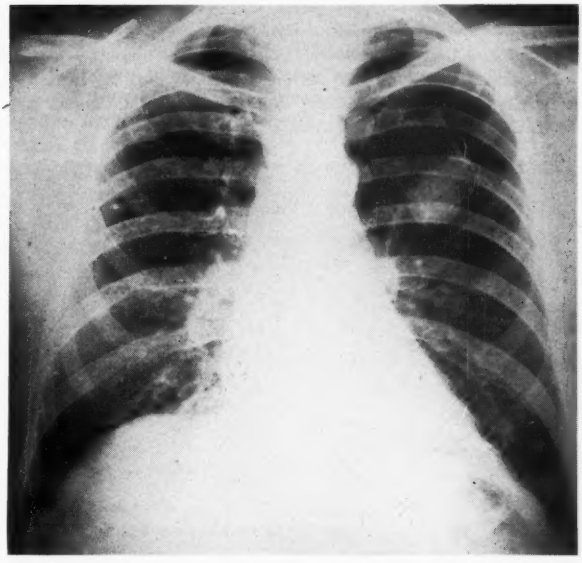

Fig. 7.—P. H. F. Discharge radiograph of chest revealed a small, rounded, discrete area of increased density in the left upper lobe near the periphery.

Fig. 8.—P. H. F. Gross specimen demonstrated a normal appearing left lung except for a firm, rounded, loosely encapsulated movable, mass 4.5 cm. in diameter in the left upper lobe. Cut sections reveal a smooth, homogeneous, yellowish surface. One portion of tumor was located just beneath and attached to the visceral pleura.

individual ligation of the hilar structures. The operative specimen consisted of an entire left lung showing a round, delimited, firm tumor mass in the parenchyma of the left upper lobe. There were no involved lymph nodes.

Microscopic Diagnosis.—On study of the microscopic sections, the only suggestive diagnostic feature was the lobulated character of the tumor, favoring a vascular unit of origin; it can therefore be classed with the capillary angiosarcomas. Malignant mesothelioma was the choice of two pathologists.

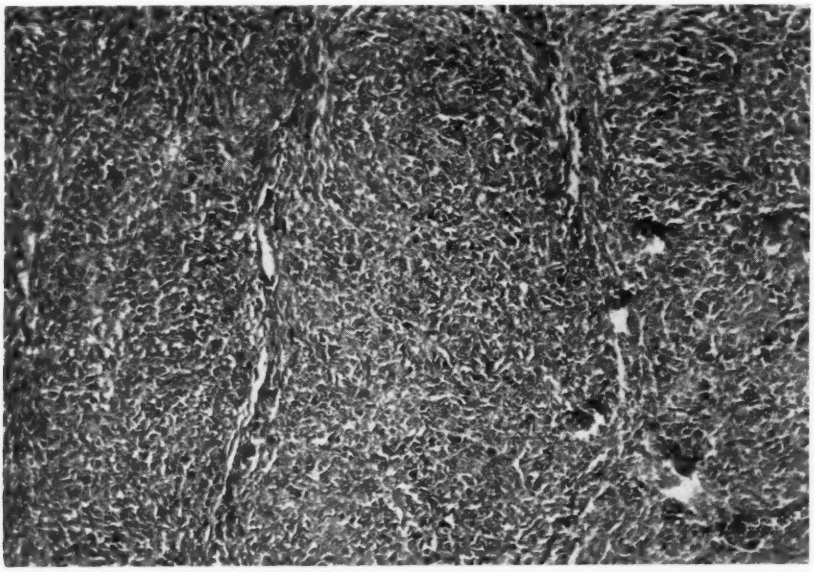

Fig. 9.—P. H. F. Microscopic study. Dr. F. W. Stewart stated that the only suggestive diagnostic feature was the lobulated character of the tumor microscopically, and he therefore favored a vascular unit organization and classed this growth with the capillary angiosarcomas. Malignant mesothelioma was the choice of two other pathologists.

CASE 10.—H. B., aged 21, complained of pain in the left chest for one year. During that time his weight had dropped from 190 to 150 lbs. A routine chest x-ray revealed a mass in the left chest wall. Aspiration biopsy of the mass revealed the tumor to be a malignant type, not classifiable.

Operation.—Resection of the third through the ninth ribs was done. The lung was adherent, but did not appear to be involved, and was not removed. The mediastinal structures were normal. The operative specimen consisted of a large lobulated mass including the fourth to eighth ribs. There seemed to be a zone of healthy tissue around the mass.

Microscopic Diagnosis.—The diagnosis was Ewing's tumor.

Comment.—This patient had chest pain for one year, and lost 40 pounds in weight before a chest radiograph was taken, revealing a lethal tumor.

CASE 11.—F. A., aged 47, complained of a cough and loss of weight. This patient was always well until January, 1943, when he developed a heavy cold and a severe cough. During the next two years, he had one cold after another which lodged in his chest, and resulted in severe coughing spells and occasional vomiting. On several occasions, he was admitted to the sick list for catarrhal fever, and once he was hospitalized for two months under a diagnosis of bronchiectasis. During this interval, bronchoscopic examination was negative and some forty chest radiographic studies were made, and finally a small area

of increased density was detected in the left lower lobe of lung. No evidence of a primary tumor elsewhere could be found, and thoracotomy was decided upon.

Operation.—Left lateral approach was used, the lung was found free of adhesions, and the hilum was normal. A smooth, round, freely movable, firm mass 4 cm. in diameter was noted in the upper inner portion of the lower lobe, and thinking this to be a benign tumor, a lobectomy was done without incident. The specimen grossly showed a circumscribed tumor arising from an ulcerated lesion in the bronchus. Microscopically, this was found to be an epidermoid carcinoma of the bronchus.

Comment.—Symptoms antedated the appearance of this patient's lung tumor by two years, and serial radiographs show the growth at its earliest stage.

SUMMARY

Of 746 cases of neoplastic disease admitted for treatment to the United States Naval Hospital, Brooklyn, thirty-three patients, one in every twenty-three, were found to have a thoracic tumor.

Twenty-three intrathoracic tumors were discovered by routine radiographic study of the chest. Five of these growths were malignant, and in each instance the patient had the advantage of an early diagnosis of his disease, which made it possible to institute prompt and definite treatment.

No instance of a surgical thoracic tumor was discovered among the Navy Wave personnel.

Thirty-three operations for thoracic tumor were performed. Three postoperative complications resulted, but there was no postoperative mortality.

Radiographic screening of a large number of healthy males has resulted in the discovery of this heterogeneous collection of twenty-three asymptomatic intrathoracic tumors.

CONCLUSION

This report adds weight to the growing impression that all persons should have routine, periodic, chest radiographs.

THE CHEST TUMOR REGISTRY

COLONEL J. E. ASH, MEDICAL CORPS, UNITED STATES ARMY*

THE purpose of this presentation is to revive interest in the Chest Tumor Registry. The war is over, and most thoracic surgeons who were in service are back in practice. It is most important that the present status of the registry and the part that thoracic surgeons can play in making it a success be known.

Many may not understand just what the purposes and functions of a registry are. A registry is a facility organized to receive cases in a specific category, to review diagnoses and obtain consultations on the pathology of difficult cases, to process all of the material so that it will always be available for study and research, and to conduct follow-up studies so that, in the course of time, the life history of as many patients as possible will be available in the particular category.

It is obvious that the success of any registry, once the necessary facilities are available, is dependent upon the cooperation of as many as possible of the persons in the particular specialty field involved. The primary purpose of the registry is to accumulate in one place as many cases in a given field as possible, in the shortest time possible, where they will be available for definitive studies. Since the data includes clinical records, x-rays, treatment, progress, and outcome, important and practical results can be obtained from the morphologic and statistical studies of the material. In addition to these long-range projects, the material is of great value in the training of general pathologists and clinicians in the specialties.

The Chest Tumor Registry is now one of fourteen that are grouped as the American Registry of Pathology, which in turn is sponsored by the National Research Council. In the present plans of the Surgeon General, this registry will be one of the four main divisions of the Army Institute of Pathology, in charge of a scientific director on a civilian status who can devote his entire time to it. Up to this point, the Director of the Institute has had to devote a limited amount of time to the registries, particularly during the past few years, although they have not been neglected. I should like to indicate the possibilities of a well-established and active registry.

The Registry of Ophthalmic Pathology, which was the first to be established, now has reports on over 20,000 enucleated eyes in its files, of which some 2,300 are melanomas of the choroid. About 800 of these have been followed for five years or more, some of them as long as twenty years. As a result of the opportunity for uniform study of this concentration of material and of correlating the life histories of such a large group with the pathology, it was

*Director, Army Institute of Pathology, Washington 25, D. C.

Read before the Twenty-sixth Annual Meeting of The American Association for Thoracic Surgery, Detroit, Mich., May 29, 30, and 31, 1946.

possible some years ago for General Callender to establish prognostic criteria on the basis of the histology. He was able to show that tumors composed of cells of a certain type were relatively benign and that other tumors containing particularly the epithelioid cells were the malignant ones. This means that when an ophthalmologist receives a report from us of malignant melanoma of the eye, cell type A, his patient has almost a certain chance of not suffering from metastasis; if it is a malignant melanoma containing epithelioid cells, the patient has a fifty-fifty chance of dying of metastasis. This information is of more than passing interest to the patient as well as to the doctor.

In the Bladder Tumor Registry, sponsored by the American Urological Association, we have over 5,000 cases. Many of these have been followed for as long as fifteen years, and these data have taught us a lot about the relationship of the histology of the bladder tumors to the clinical course and outcome. We have learned for example, that what is considered generally by urologists and pathologists to be simple, benign papilloma may very well undergo a malignant transformation and the patient may even die of metastasis. We have long since stopped calling these simple papillomas.

The accumulation of treatment data in 500 cases coming from different clinics has enabled us to evaluate the efficacy of treatment advocated by various groups. For example, one group depends upon massive irradiation, another group depends predominantly upon surgery. The results of these studies had their influence upon the form of treatment in certain parts of the country. There are similar opportunities in the field of thoracic surgery, but wholehearted cooperation in registering cases, furnishing adequate data, and assisting in the follow-ups are required.

Registering cases does not deprive the surgeon of any use he may wish to make of them. Any specific use made of the case reports is made with his permission. One great advantage of registering cases is that the reports are always available and not dependent upon the vagaries of changing personnel or policies, as may be the case in civilian institutions. We realize that it is something of a nuisance to prepare cases for registering. We have a special blank that is a help in furnishing clinical data. We do want an operative report, in order to orient properly the lesion and procedure, and, of course, the x-rays, which are of particular importance to the case records. We want originals to copy and return. Also, we have to have all of the material the surgeon can spare. It is frequently necessary to make special stains, and if the case is appropriate for study purposes, to cut a number of slides for study sets.

In spite of the fact that many thoracic surgeons have been on active duty and that those who were not have been too busy in civilian clinics to register cases, the registry has not been asleep. The United States Army is the only armed force in the world that provides for such centralization of its pathology. This system was established in the 1920's, so that when mobilization jumped the army from 125,000 to a million men, it was necessary only to expand the mechanism to receive and process the material from the greatly increased number of army hospitals. When hostilities opened and the armies invaded all quarters

of the globe, facilities were expanded to take care of the hospitals in the theaters of operation. We were very fortunate in having the generous and intelligent cooperation of practically all the pathologists in the army, and for particular purposes we now have at the institute all of the autopsies that were performed by, and on, military personnel in any part of the world. In addition, we also have the large majority of all significant surgical material. This is particularly true in the field of chest surgery. Some who were in service have been concerned about the fate of that material. If it had not been for this centralization of pathology, much of it would undoubtedly have been lost. As it is, in most instances, if the surgeon can furnish the name of the patient, we can give information about his case.

At the peak, we were receiving over sixty autopsies a day, seven days a week, and an equal number of significant surgical specimens. The intake is still at a high level because the hospitals that are closing are sending in their accumulations. There is little likelihood that receipts will dwindle to the comparative trickle that they were before the war, since, by agreement between the Secretary of War and the Director of the Veterans' Administration, we are functioning for the veterans' hospitals as for the army. This is of particular importance because it assures follow-up in a great many cases represented by surgical specimens at the institute.

In addition to this enormous amount of pathologic material which has been collected, there is also a tremendous amount of illustrative material. Early in the war we organized, equipped, and trained units made up of clinical photographers and medical artists, and sent them to all the theaters. We were also practically in charge of the clinical photography in the general hospitals in this country. From all of these sources, black and white and kodachrome stills, kodachrome movies, and medical artists' drawings poured back to the Institute. There are well over 100,000 black and white pictures, some 20,000 kodachromes, many of the clinical pictures, and 100,000 feet or more of colored movies illustrating all phases of Medical Department activities, but more especially clinical subjects and operative procedures. It is our function to make all this material, pathologic and illustrative, available for training and research not only to the army but also to the civilian profession.

To give an idea as to what this material means in thoracic surgery, the following table is presented:

Teratomas, mediastinal	29
Teratomas, lung	17
Carcinoma, lung	769
Superior sulcus tumors	6
Cysts of lung	64
Neurofibroma, pleura and mediastinum	23
Lobectomies for tuberculosis	37

Several studies have already been completed on this material, one on the teratomas of the mediastinum by Major Schlumberger[1] of the Institute Staff, who approached the subject from the unique angle of embryology. We have

had a particularly large group of bronchial adenomas which are of great importance to thoracic surgeons. Major Holley, who is a chest internist as well as a pathologist, has made an interesting study of this group that will appear shortly in the literature.[2] The army is one of the pioneers in lobectomies for tuberculosis, and that accounts for the considerable group of cases in this category.

One of the important acquisitions to the registry was the material accumulated during the earlier stages of the Chest Tumor Registry by Dr. Andrews. There are about 148 cases. Unfortunately, while the records are very well prepared, there are only thirty some that are represented by tissue. These have been incorporated into the present registry. Records without supporting pathologic material are not of much value in the registry activity.

I hope that thoracic surgeons take the Registry seriously and help make it one of the most active of the group. Great good has come to other special fields from their registries, and I am sure that material benefit can come from it. If there is anything regarding the Registry that is not clear, simply direct the inquiry, or make any suggestions to The Director, Army Institute of Pathology, Washington 25, D. C.

REFERENCES

1. Schlumberger, H. G.: Teratomas of the Anterior Mediastinum, Arch. Path. **41**: 398-444, 1946.
2. Holley, S. W.: Bronchial Adenomas, Military Surgeon **99**: 528-554, 1946.

A REPORT OF 196 LOBECTOMIES PERFORMED AT KENNEDY GENERAL HOSPITAL CHEST SURGICAL CENTER FROM 1943 TO 1946 WITH ONE DEATH

RICHARD H. MEADE, JR., M.D.,* CHICAGO, ILL., LIEUTENANT COLONEL EARLE B. KAY, MEDICAL CORPS, ARMY OF THE UNITED STATES, AND MAJOR FELIX A. HUGHES, MEDICAL CORPS, ARMY OF THE UNITED STATES

THE operation of lobectomy has been performed for so many years with such low mortality that there is little justification for the report of another series just because there was only one death in 196 consecutive operations. Churchill,[1] in 1936, was able to report that he had performed sixty-six consecutive lobectomies with only one death. Since that time, other surgeons have recorded comparable figures. As the war is now over and most of the army hospitals have been closed, it is thought worth while to review the experiences with lobectomy in one of the army's chest surgical centers in this country. A comprehensive, official report of the work in all of these centers will be published later. The present report has to do with only one aspect of this work, carried out in one of the centers, Kennedy General Hospital in Memphis.

Soon after its opening in January, 1943, Kennedy General Hospital was designated as a chest surgical center. To such centers were sent patients with chronic chest diseases for whom there was any possibility of surgical therapy. They came from all parts of this country and from overseas if their condition was such that return to duty could not be expected within a reasonably short period of time. Battle casualties accounted for the majority of the cases, but the great bulk of the operative work was done for conditions unrelated to warfare. Lobectomy was the commonest major operative procedure. Between November, 1943, and April, 1946, 196 lobectomies were performed on 190 patients with one death following the fourth operation. The operators were the three authors and three other transient members of the staff† (Table I).

TABLE I. SUMMARY OF LOBECTOMIES PERFORMED FROM NOVEMBER, 1943, TO APRIL, 1946

Total number of patients		190
Total number of lobectomies		196
Bilateral lobectomies	4	
Unilateral, same patient	2	
Total	6	
Deaths		1

From the Chest Surgical Section, Kennedy General Hospital, Memphis, Tenn.

Read at the Twenty-sixth Annual Meeting of the American Association for Thoracic Surgery, Detroit, Mich., May 29, 30, and 31, 1946.

*Formerly Lieutenant Colonel, Medical Corps, Army of the United States, and Chief, Chest Surgical Section, Kennedy General Hospital, Memphis, Tenn.

†Major Theodore R. Hudson, Major Julian Johnson, and Captain Spires Whitaker.

Age of Patients and Indications for Operation.—As would be expected, the patients were almost all young men in good general condition. Twelve were under 20 and only four were over 40, the majority being between 20 and 30 years old (Table II).

TABLE II. AGE DISTRIBUTION OF PATIENTS HAVING LOBECTOMIES*

AGE	NUMBER PATIENTS
Under 20	12
20-30	126
30-40	48
40-50	4
Total	190

*Four patients had bilateral lobectomies, and two had two unilateral lobectomies.

Bronchiectasis was the chief indication for operation, being responsible for 161 lobectomies. Decision for surgery was based on bronchographic demonstration of the disease together with definite symptoms that had persisted for a reasonable period of time in spite of active medical treatment. This conservative therapy included treatment of associate nasal accessory sinus disease, postural and bronchoscopic drainage, and penicillin by all routes. In no instance was operation refused because of the severity of the disease unless so much pulmonary tissue was involved that the equivalent of the two upper lobes, exclusive of the left lingula, could not be preserved. Twenty-seven of the patients had bilateral bronchiectasis. Although the indication for operation was bronchiectasis in 161 instances, in one of the lobes the condition was found to be adenomatosis, and in one lobe squamous cell carcinoma was found in a bronchiectatic cavity. Only 156 patients had these 160 lobectomies. Four of the patients had bilateral lobectomies done at Kennedy. One other patient had had the right middle and lower lobes removed elsewhere by one of us (E. B. K.) and had the left lower lobe and the lingula of the left upper removed at Kennedy.

Pulmonary cyst was the next most frequent diagnosis before lobectomy and was responsible for twenty-two operations. In four instances this diagnosis was not confirmed at operation. In two instances the cyst was found to be due to tuberculous cavitation, in spite of the fact that prolonged and careful studies to exclude this diagnosis had been made over a period of months; in one, the cyst was found to be bronchiectatic and in the other there was a large, degenerated neurosarcoma. This last patient was operated upon entirely because of the presence of a large shadow in the left upper lobe region in the separation roentgenogram. He had had absolutely no symptoms. Operation for cyst was only recommended when there were associated symptoms, when the diagnosis was in doubt, or when, because of evidence of bronchial communication, it was feared that infection would later develop.

In two patients the indication for lobectomy was the finding of a bronchial adenoma. This diagnosis was confirmed in each instance and in one other lobe, in which it was not previously suspected, an adenoma was found.

Chronic suppuration was the indication for lobectomy in nine patients, in one of whom the process was found to be due to actinomycosis and in another, secondary to bronchial obstruction caused by an adenoma.

Actinomycosis was the diagnosis in two of the lobectomies which were performed on the same patient. At the first operation, the right upper lobe and part of the lower were removed. Following recovery from this operation, evidence of spread into the lower lobe was found, and the remainder of the lung was then removed with apparent cure of the patient. (Tables III, IV, V, and VI.)

TABLE III. INDICATIONS FOR LOBECTOMY

Bronchiectasis	161
Cyst	22
Chronic suppuration	9
Bronchial adenoma	2
Actinomycosis	2
Total	196

TABLE IV. DISEASES FOUND IN THE LOBES REMOVED AT OPERATION

Bronchiectasis	160
Cyst	18
Chronic suppuration	7
Bronchial adenoma	3
Actinomycosis	3
Tuberculosis	2
Neurogenic sarcoma	1
Carcinoma	1
Adenomatosis	1
Total	196

TABLE V. LOBECTOMIES PERFORMED FOR BRONCHIECTASIS

DISTRIBUTION OF DISEASE		LOBECTOMIES	DEATHS
Unilateral	129	156	1
Bilateral	27	4	
Total	156	160	1

TABLE VI. DISTRIBUTION OF LOBES REMOVED AT OPERATION

LOCATION	NUMBER CASES	
Left		126
Upper	4	
Lower	85	
Lower and lingula	35	
Middle and lower (situs inversus)	1	
Anomalous lower	1	
Right		70
Upper	5	
Upper and part lower	1	
Middle	13	
Middle and lower	16	
Lower	35	
Total		196

Results.—All patients, with one exception, recovered fully from their operations. Death occurred in the fourth patient in the series, twenty hours after operation. Complications of more than transient significance occurred in twenty-seven cases; fifteen of these were due to empyema. Immediately after their lobectomies seven patients developed jaundice which was associated with evi-

dence of liver damage and could not be ascribed definitely to transfusion reactions. Hemothorax, requiring repeated aspiration and finally drainage, occurred after one lobectomy. Pneumothorax unassociated with evidence of infection occurred in two patients and responded promptly to closed drainage. In one patient, evidence of a focal brain lesion developed three days after lobectomy and, at operation six weeks later, a small, cystic area was found which was thought to have been the result of an embolus. Atelectasis of transient nature occurred in a number of cases but responded promptly to transnasal, tracheal aspiration except in one instance. In this case it was necessary to bronchoscope the patient and, even then, the inspissated plug of secretion was aspirated with great difficulty from the left upper lobe bronchus. All wounds healed by primary intention except those associated with drainage.

Preoperative Management.—Only in patients with bronchiectasis or other suppurative disease was there any special preparation for operation. In these patients, the chief problem was to control the inflammatory process as far as possible and to get them into the best general condition. Most of our patients were already in good general condition and raised less than 4 oz. of sputum a day. These were operated upon as soon as the lipiodal remaining in their good lobes after bronchography had largely disappeared. Usually this meant a wait of at least a month, during which time the patient was allowed to go home. For those patients who had more sputum and evidence of active infection, postural drainage, bronchoscopic aspiration, penicillin, and high vitamin intake were used. Penicillin was administered by all routes but was more effective when injected directly into the trachea or given by the aerosol aspiration method. In a few instances the addition of sulfadiazine was found to be of value. These measures were continued until it was thought that maximum improvement had been secured. As the hospital was located in a mild climate and as air conditioned rooms were available after the first year, no operation was postponed because of the weather.

The immediate preoperative preparation of the patient for lobectomy had to do with insuring the most effective clearing of the bronchial tree of secretions by his own efforts, and the establishment of an effective penicillin blood level. The minimum amount of penicillin given prior to a scheduled lobectomy was 100,000 units by the intramuscular route, given during the twelve hours immediately preceding the operation. Depending upon the nature of the case, larger amounts were given over a longer period. Bronchoscopy was rarely used just before the operation as it was thought to be unnecessary and because it greatly delayed the induction of satisfactory anesthesia. In the cases in which it was used, the patients had such flooding of the tracheobronchial tree with blood or pus or both that catheter aspiration through the intratracheal tube had been ineffective. Preanesthetic medication consisted of Nembutal grains 1.5 two hours before operation, and morphine sulfate grains $\frac{1}{6}$ with scopolamin, or atropine sulfate grains $\frac{1}{150}$ one-half hour later.

Operation.—All patients were operated upon under intratracheal ether-oxygen anesthesia with nitrous oxide-oxygen induction. After the first few lobectomies, respirations were controlled by the anesthetist with the aid of man-

ual pressure on the anesthesia bag. Packing of the pharynx with gauze rather than the use of an inflatable cuff on the intratracheal tube was relied upon to maintain a tightly fitting airway and to prevent the entrance into the trachea of oral and pharyngeal secretions. Aspiration of the trachea and bronchi was carried out by means of a soft rubber catheter at first, and later by means of a semirigid catheter. Care was taken to prevent the aspirating tube from being inserted too deeply. In one instance the aspirating catheter was forced through the bronchus of the lower lobe that was being removed. After this experience greater caution was used.

Before the incision was made, an intravenous infusion was started with normal salt solution, and then blood containing 100,000 units of penicillin was given during the operation. The amount of blood given varied from 1,000 c.c. to 3,500 c.c., with 1,500 c.c. as the usual amount.

In general, for lower lobe excisions the patients were operated upon in the lateral position, but in a small series they were placed on their backs with the involved side slightly elevated. In this latter group the chest was opened through the bed of the anterolateral segment of the fifth rib, and this approach was used primarily in patients with a large amount of secretion. As the exposure obtained was not entirely satisfactory at times, this approach was abandoned in favor of the approach through the bed of the sixth or seventh rib, which had been resected for most of its extent. For middle lobe excisions, the approach was anterolateral through the bed of the fifth rib. For upper lobectomies, the anterolateral approach was used as often as the lateral. For removal of the left upper lobe, it was felt that the easiest approach was through the fissure between the lobes and that the lateral approach through the bed of the fifth rib gave the best exposure.

Except for the first two lobectomies, individual vessel ligation technique was used exclusively. In the first case there was so much induration of the tissues at the hilum of the lobe that dissection of the vessels was thought to be unwise. In the other instance, a middle lobe, the site of chronic suppuration, was removed, and although the vessels were not isolated, very little lung tissue was left behind. In neither instance did empyema follow the operation. In developing the fissures between the lobes, care was taken to avoid injuring the good lobe, and raw areas were closed with continuous sutures of fine catgut. In patients with much secretion, the bronchus was closed as soon as possible, but this was rarely accomplished before the arteries were divided. The inferior pulmonary vein was the last vessel ligated, as it was thought that the danger of embolism from the involved lobe was less important than the technical disadvantage of engorgement of the lobe. All major vessels were divided between ligatures and suture ligatures of silk. The bronchus was carefully isolated and divided between clamps in order to minimize the contamination of the pleural space by the spilling of bronchial contents. Careful walling-off of the area with gauze was done before the bronchus was divided, culture was taken from the bronchial stump, and, after swabbing dry, penicillin was applied. Several vertical mattress sutures of fine silk were passed through the stump proximal to the clamp, which was then removed and the crushed segment of bronchus excised. Closure of the stump was

then completed with interrupted sutures of fine silk. The ends of the mattress sutures were left long for use later in holding the bronchial stump in place under the pleural flap. A flap of pleura and underlying tissue was then elevated from the area just posterior to the stump, followed by careful covering of the stump. The importance of this procedure has been demonstrated by Reinhoff and associates,[2] and Sweet[3] and we agree that it is the most important single step in the prevention of bronchial leakage with its resultant empyema. When the bronchial stump was covered and the remaining lobe freed from any adhesions that might interfere with its full expansion, a stab wound was made in the midaxillary line, and through the ninth or tenth interspace a semirigid, fenestrated, rubber drainage tube was inserted until the end came in contact with the posterior wall well below the site of the bronchial stump. The tube was held in place by means of a single suture of catgut passed through the deep tissues of the chest wall and tied around the distal segment of the tube. This tube was fixed to the skin by means of a silk suture and it was then connected with a water trap. Before final closure of the chest wall, the remaining lung was fully inflated by aspiration of the air from the pleural cavity and by increasing the pressure in the tracheobronchial tree. Usually, 100,000 units of penicillin were used for the initial flooding of the bronchial stump and for the pleural cavity as a whole. One operator injected some of the penicillin directly into the tissues around the bronchial stump. As soon as the chest was closed, the patient was turned on his back and bronchoscoped. The direct visualization of the tracheobronchial tree and the aspiration of any material was considered of great importance in minimizing the danger of bronchial obstruction developing later.

Postoperative Management.—Maintenance of a clear airway was the most important feature in the immediate postoperative period, and all of the personnel on the ward were instructed in the steps necessary to accomplish this. Transnasal aspiration of the trachea with a catheter was used until the patient was conscious enough to take an active part by coughing. Except in rare instances when the security of a large vessel was uncertain, patients sat up in bed as soon as conscious and were made to cough. When adequate support was provided, the patient was almost always able to cough effectively and clear the airway. If not, the irritating effect of a catheter passed into the larynx was nearly always successful in precipitating effective coughing. Nurses and other attendants were drilled in the importance of a clear airway, and the dramatic improvement in a patient's condition following the removal of a bronchial plug was not forgotten.

Oxygen was given by way of a nasal catheter in practically all patients after air conditioned rooms became available. This method was preferred because it made it easier to handle the patient and because it was considered more efficient than a tent. The patients seemed to prefer this method and in no instance was the supply of oxygen thought to be inadequate. Except in rare instances, oxygen was not given after the first twelve or eighteen hours, as we could see no advantage to be gained by prolonging its use when the patient was able to breathe in comfort without it and showed no evidence of cyanosis. When the weather was hot and an air conditioned room was not available, the tent was used for its cooling effect.

As was described earlier, the drainage tube was connected with a water trap bottle before the chest wall was closed. A Y-connecting tube with a short piece of rubber tubing was incorporated in the system to provide a ready means of irrigating the tube should the necessity arise. Usually the pleural cavity was filled by the re-expanded remaining lung tissue within the first twelve hours and the tube was removed on the second postoperative day. Decision as to the time of removal of the tube was based on the cessation of respiratory movements in the patent drainage tube, the presence of clear breath sounds over the operated side, and the roentgenographic evidence of re-expansion of the lung. It was thought unwise to remove the tube until these findings had been present for at least twelve hours. In those cases in which it was thought that overdistention of the remaining lung tissue would be necessary to fill the pleural space because of the removal of more than one lobe or because of an unusually large lobe, the diaphragm on that side was paralyzed by crushing the phrenic nerve in the neck as soon as it seemed certain that full aeration of the lung had taken place. This was rarely done before the fifth postoperative day or while the drainage tube was still in place. Simple water trap drainage was used in all cases after the first few, as it was obvious that suction was not necessary to aid in prompt re-expansion of the remaining lung and because it was felt that observation of the respiratory fluctuation of the fluid in the tube gave important information about the pleural cavity.

Early active movements were insisted upon and patients were allowed to stand with support the night of the operation if they needed to do so to void. Almost every patient was fully ambulatory by the end of the first week, with all skin sutures out and the wound in good condition. Aside from making the patients cough at frequent intervals during the immediate postoperative period and getting them out of bed within the first few days, no formal course of exercises was given except for those patients who would not move about actively of their own accord.

Penicillin was continued by intramuscular injection for the first five to seven days in practically all cases. It was not continued after there was evidence of obliteration of the pleural space by the reexpanded lung and after the temperature was normal. The dosage used was 25,000 units every three hours, unless conditions called for more. A number of patients developed severe urticaria after receiving the penicillin for several days and no treatment for this distressing condition was found. Spontaneous clearing occurred a variable number of days following the cessation of its administration. In no instance did it appear in a case for which penicillin was considered of great importance, under which circumstances the drug would have been continued in spite of the urticaria.

Paralysis of the diaphragm was induced in the majority of our patients, either to prevent overdistention of the remaining lung tissue, to relieve deep-seated pain or tightness, or to abolish the pull of the moving diaphragm on a bronchial stump which had not been satisfactorily covered with pleura. The first phrenic paralysis was induced in December, 1944, in a patient who had

had a left lower lobectomy for bronchiectasis but who persisted in having some productive cough. A bronchogram had shown the lingula bronchi to have assumed a vertical position and to be somewhat dilated. Hoping that paralysis of the diaphragh might allow these bronchi to assume a more normal position and thus drain better, operation was done. The productive cough promptly disappeared not to return, but a repetition of the bronchogram showed no change in the position of the bronchi. However, immediately after the phrenic nerve was blocked the patient felt more comfortable in his chest, could breathe more deeply, and could cough more effectively. Following this experience, phrenic nerve block was used in all cases after the remaining lobe had become fully aerated if the patient had persistent deep pain in his chest or a sense of tightness. In every instance there was immediate relief of the symptoms and the patient felt that he could breathe more fully. It would seem probable that the improvement in breathing in our first case brought about better bronchial drainage and thus caused disappearance of the productive cough.

Complications.—As was stated in the beginning of this report, there were complications of more than transient nature in twenty-seven cases (Table VII). The most important of these was empyema, which developed in fifteen patients. All but four of these were definitely secondary to leakage from the bronchial stump and were associated with bronchial fistulas. In none of these cases was it possible to secure adequate covering of the bronchial stump with pleura. In the four patients who developed empyema without evidence of a bronchial fistula, two had had a considerable amount of lung tissue cut across in establishing fissures and had developed severe jaundice, but all had had adequate covering of their bronchial stumps with pleura. Also in one of these two jaundiced patients, the middle and lower lobes had been removed, and the empyema developed after the drainage tube had been withdrawn and phrenic paralysis had been induced to decrease the size of the remaining pleural space. Infection of the jaundiced fluid reaccumulating in the space resulted. Our experience with these complications impressed upon us the great importance of pleural covering of the bronchial stump and the rapid obliteration of the pleural space by means of the re-expanding lung.

TABLE VII. COMPLICATIONS FOLLOWING LOBECTOMIES

COMPLICATIONS		NUMBER CASES	
Pulmonary and Cerebral Edema			1
Other Complications Followed by Recovery			
Conditions requiring drainage			19
Hemothorax		2	
Pneumothorax		2	
Empyema		15	
Without bronchial fistula	4		
With bronchial fistula	11		
Jaundice			7
Cerebrovascular accident			1
Atelectasis requiring bronchoscopy			1

Two patients developed apical pneumothorax several weeks after lower lobectomy and required closed drainage to correct the condition. No infection developed in either case.

In two instances, hemothorax developed after withdrawal of the drainage tube and, following failure of aspiration to eradicate the condition, closed drainage was effective in two weeks.

Jaundice of varying severity appeared in seven patients and, although associated with evidences of temporary disturbance of liver function, no exact diagnosis of its nature could be made. It appeared within two or three days after operation and in one case the icterus index went to 207 units. All had some abdominal discomfort and anorexia, but none were seriously ill. There was no evidence of transfusion reactions, although all of the patients had had large quantities of blood during the operation. The jaundice did not persist for more than three weeks in any case.

One patient developed evidence of a focal brain lesion three days after operation and was treated with penicillin and streptomycin on the basis of the condition being due to a septic embolus. Operation sixteen days after lobectomy revealed a small cystic area without evidence of infection. No exact diagnosis was made but the patient made a complete recovery.

The one death occurred in a patient aged 37 who had had bronchiectasis of the right lower lobe for many months with repeated hemoptyses. The operation, the fourth in our series, was difficult and required much time. Anesthesia was unsatisfactory because of difficulty in maintaining a clear airway, and death followed twenty hours later as a result of cerebral and pulmonary edema. This was considered to have been a preventable death.

COMMENT

This report has been made in order to place on record the series of lobectomies performed at one of the Army's chest surgical centers in this country. The low mortality rate should be ascribed to the youth and good general condition of the great majority of our patients, and to the application of modern techniques by an enthusiastic group working together as a team.

SUMMARY

1. Between November, 1943, and April, 1946, 196 lobectomies were performed on 190 patients at Kennedy General Hospital, Memphis, with one death.

2. All patients except four were under 40 years old, the majority being under 30.

3. Lobectomy was performed for the following conditions: bronchiectasis in 160; pulmonary cyst in eighteen; chronic suppuration in nine; bronchial adenoma in three; adenomatosis in one; tuberculosis in two; neurogenic sarcoma in one, and actinomycosis in two.

4. Bilateral lobectomy for bronchiectasis was performed on four patients. A fifth, who had had his right lower and middle lobes removed elsewhere, had his left lingula and lower lobe removed at Kennedy by the same surgeon.

5. Preoperative preparation made use of penicillin in all cases, and in all patients with an infectious process it was used by all routes until the acute

process was controlled as far as possible. Intratracheal instillation was found to be of particular value. Postural drainage and bronchoscopic aspiration were also used.

6. Intratracheal ether-oxygen anesthesia was used in all cases. After the first thirty operations, respirations were controlled by the anesthetist.

7. Individual vessel ligation technique was used after the first two cases. Silk technique was used throughout.

8. All patients were bronchoscoped at the end of each operation.

9. Closed drainage with a water trap was used and the tube was connected with the bottle before closure of the chest wall. Drainage was usually continued for two days.

10. Oxygen administration by way of a nasal catheter was routinely used but was usually discontinued after twelve to eighteen hours.

11. Maintenance of a clear airway was considered the most important feature of the immediate postoperative period. Transnasal tracheal aspiration was used until the patients could cough actively.

12. Early active movements were insisted upon. Practically all patients were fully ambulatory by the end of the first week.

13. Phrenic paralysis was induced in the majority of patients after full aeration of the remaining lung was regained, for three indications. These were in patients who had had more than one lobe or a large lobe removed when overdistention of the remaining lobe was to be avoided by decreasing the size of the pleural space, in patients with deep-seated pain or tightness, and in order to diminish the pull on bronchial stumps with unsatisfactory pleural covering.

14. Complications of more than transient nature occurred in twenty-seven cases. Empyema accounted for fifteen, an incidence of 7.6 per cent. Jaundice of undetermined origin appeared in seven. Pneumothorax, requiring a short period of drainage, appeared several weeks after operation in two. Hemothorax requiring drainage occurred in one. Atelectasis necessitating bronchoscopic aspiration developed in one, and cerebral embolism followed by recovery was encountered in one.

15. Death occurred in one patient twenty hours after lower lobectomy for bronchiectasis, giving a case mortality of 0.52 per cent and an operation mortality of 0.51 per cent.

16. The work herein reported is an example of that done in the army chest surgical centers in this country.

ADDENDUM

Since the completion of this article, the total number of lobectomies performed up to the termination of the chest surgical section at Kennedy General Hospital in May, 1946, was increased to 236 by Lieutenant Colonel Kay and Major Hughes, without further mortality.

Without the efficient help of the anesthetists, Captain Frank Galioto, Lieutenant Darrell Faubion, and Lieutenant Thomas McCrory, these good results could not have been obtained.

The intelligent and faithful nursing was of great importance, as was the cooperation of all who had to do with the care of the patients. The enthusiastic support of the commanding officers, Brigadier General Royal Reynolds and Colonel Albert McEvers also contributed greatly.

REFERENCES

1. Churchill, E. D.: Bronchiectasis; Physical and Psychological Manifestations, New England J. Med. **218:** 97, 1938.
2. Rienhoff, W. F., Jr., Gannon, James, Jr., and Sherman, Irwin: Closure of the Bronchus Following Total Pneumonectomy; Experimental and Clinical Observations, Ann. Surg. **116:** 481, 1942.
3. Sweet, R. H.: Closure of the Bronchial Stump Following Lobectomy or Pneumonectomy, Surgery **18:** 82, 1945.

DISCUSSION

DR. RICHARD H. OVERHOLT, Brookline, Mass.—This amazing record is truly breathtaking, and, I think, deserves particular praise. It is too bad that all the medical men of this country are not here today to hear what has been accomplished with regard to the salvage of such a large group of patients.

At this time we might call attention to the pattern of the disease and emphasize that bronchiectasis is not truly a lobar disease but is essentially a segmental disease. In our own series of cases, we found that the disease was multisegmental and bilateral in 30 per cent. I notice that in Dr. Meade's group bilateral disease was present in 21 per cent.

Some attention to the segment of lung has been given by Nelson, Churchill and Belsey, by Blades, and more recently by Boynton.

It is time, I think, to consider the segment of the lung as a surgical unit in the treatment of bronchiectasis rather than the use of the lobe as a surgical unit. This applies particularly to the management of bilateral disease.

I should like to discuss briefly the technique that we have employed in the past year in the treatment of bilateral bronchiectasis. Lobes are taken apart on either side by a new method of dissection, developing the intersegmental plane of cleavage without the use of clamps, without the use of suture material, and without traumatization of the adjacent segment.

(Slide.) The appearance on the right is an artist's interpretation of a colored photograph of the picture that we so often see when the chest of a patient is opened for treatment of bronchiectasis of the basal segments and the lingula. This exposure has been obtained with the patient lying in the prone or face-down position. Both the upper and lower lobes are within full view. The superior division of the lower lobe has undergone compensatory emphysema. The apicoposterior and anterior segments of the upper lobe have likewise undergone compensatory enlargement. Often it is necessary to lift the lower lobe up to visualize the diaphragmatic surface before any atelectatic lung can be seen. Healthy, aerated segments practically fill the entire hemithoracic space.

The drawing on the left shows the final result in our routine operation for segmental bronchiectasis. There has been a conservation of the superior segment of the lower lobe, which is overdeveloped and able to function, as well as a conservation of the upper two segments of the upper lobe. These remaining segments easily fill the hemithoracic space without further overdistention.

(Slide.) The first step is to ligate the basal artery. If one contemplates the removal of the lingula, it is convenient to ligate the basilar artery and the lingular artery at this time. Step two is the treatment of the vein. The lobe is then turned over and the basilar vein is identified and ligated. Great care should be taken to avoid injury of the superior segmental vein.

(Slide.) Step three is the division of the bronchus. Here, the bronchus has been identified, and in this case it was approximately the same size as the superior divisional bronchus. The bronchus is divided and contamination is avoided if possible. Three of the four binding structures have now been released. We have come to find that segments are held

in place by four structures—the bronchus, the artery, the vein, and the visceral pleura. The anesthetist then inflates the lung. The line of demarcation can be readily seen between the healthy segment and the basal segments. Step four. The visceral pleura is divided very carefully by incising just the visceral pleura itself. That incision starts on the mediastinal surface posteriorly, goes around the lateral surface of the lobe, around the anterior surface, and back to the anterior mediastinal surface.

After the fourth sustaining structure; i.e., the pleura, has been divided, the rest of the dissection is rather simple in that the lobe virtually falls apart by gentle section with the thumb and forefinger.

(Slide.) We have been surprised to find that the intersegmental plane is not firmly bound but can be developed by gentle blunt dissection. Arteries or bronchi do not traverse the plane. Usually two to four veins are found to cross. Fine mosquito hemostats are used on the venous branches as they are exposed. Gradually the bronchi separate and are pulled out. The substance of the lung melts away between thumb and forefinger.

We found in trying to do a segmental resection with the clamp method that the clamps do not find the proper anatomical plane of cleavage. One includes either diseased bronchi or healthy bronchi. The remaining segment is traumatized by the clamps and constricted by sutures.

(Slide.) One case will illustrate this method. This patient with bilateral bronchiectasis had been sick for seven years. There was found to be involvement of the anterior segment of the right upper lobe, the right middle lobe, and the basal segments of the left lower lobe. So the problem was to remove the basal segment of the left side and three months later the right middle lobe and the anterior segment of the right upper lobe. Bronchograms before and after the bilateral segmental resections are shown.

We have carried out segmental resection in about twenty-five cases, starting first on bilateral cases where a conservation of every healthy pulmonary segment was paramount. We now feel confident in the safety of this procedure and are applying it in unilobar disease, particularly on the left side, where so often the lingula is involved. It is desirable to save as much functioning lung as possible. If one removes all of the lower lobe and the lingular division, one ends up with just two divisions of the upper lobe, the apicoposterior and anterior, to fill the left chest. Frequently, only the inferior branch of the lingular bronchus need be removed. On the right, the middle lobe can be divided and only a diseased branch resected. This operation has been applied in other cases. For example; in cases of tuberculosis where resection of the upper lobe is indicated and you find the superior division of the lower lobe to be involved it is possible to remove that segment of the lower lobe with the upper.

We have also removed the apicoposterior segment on the left side in two instances, one for a giant cavity and one for tuberculoma.

We have removed the lingula in treating a metastatic tumor, removed the superior segment containing a benign tumor and other individual segments for cystic disease.

I thought it might be appropriate at this time to call your attention to this particular refinement which may add much to the conservative treatment of bronchiectasis, particularly in the bilateral case.

DR. DAVID H. WATERMAN, Knoxville, Tenn.—This is really a discussion of Dr. Overholt's discussion, but I would like to take the opportunity of saying that I think this series of Dr. Meade's at Kennedy General is a brilliant piece of work. I have seen some of it done.

What Dr. Overholt described in doing segmental resection by fingertip peeling away of the involved segments works just as well as he says it does. I have tried several cases since I first talked with him concerning it, and am enthusiastic about the technique.

The only variation I might suggest is that it is not necessary, I think, to divide first the visceral pleura between the uninvolved and the involved segments. We have found that

by using the distal stumps of the hilar structures for traction, the involved segment can be easily peeled outward to the visceral pleura. The pleura can then be divided without the slightest difficulty, exactly where the surgeon wishes to divide it.

I think it would be possible, if we desired to do so, even to leave a large flap of pleura peeled from the involved segment sufficiently large to swing back over the denuded area of the remaining segments. However, there is practically no surface bleeding with this segmental type of resection, and I doubt if such a procedure is really necessary.

DR. DANIEL A. MULVIHILL, New York, N. Y.—One cannot help being impressed with this remarkable record in such a large series of cases of major surgical procedures in the thorax as Dr. Meade has had, and I know that at the other Army Chest Centers, Dr. Blades and his associates, Dr. Grow and his associates have comparable series.

I have had an opportunity for a very brief time in 1945 to take part in some of the work at Fitzsimmons, having, in the prewar period, followed with admiration the development of Dr. Churchill's very fine series of lobectomies for bronchiectasis. Knowing how sick some of these patients were, what care was necessary in the selection of cases, particularly the bilateral ones, and what a difficult matter it was to prepare patients for operation, and then having lost track of developments during my two years of overseas service, I was quite impressed by the number of cases of bronchiectasis that showed up in the Army Chest Centers. That is more impressive when we consider that here is a group of young, healthy men who were thoroughly screened by several examinaitons before their induction, and by x-rays, and some of whom had undergone a very strenuous active campaign.

A point I would like to bring out, and about which I would like to ask Dr. Meade, and would also like to hear discussed by Dr. Grow, Dr. Blades, and Dr. Churchill, is: What does this tell us about the etiology of bronchiectasis? Did these cases of bronchiectasis develop as a result of interim infections in these supposedly healthy young men since they entered the war service?

The other point that I would like to hear discussed is the matter of clinical and anatomic bronchiectasis. In the cases I was able to observe at Fitzsimmons there was no question as to the anatomic bronchiectasis demonstrated by lipiodol bronchograms. However, these cases in the large majority, did not show the picture of clinical bronchiectasis that we would have expected from the type cases that Dr. Churchill had operated on prior to war.

The point I would like to bring up here and hear discussed is: Is anatomic bronchiectasis in itself, even if demonstrated by lipiodol bronchograms, an indication for lobectomy? In many cases, if this point of view is taken, operation must be from the standpoint of prophylaxis, because these patients with anatomic bronchiectasis only are not the "social outcast" type that we used to meet in the early days of lobectomy for bronchiectasis.

DR. DEAN COLE, Richmond, Va.—Dr. Meade and his associates are to be congratulated on an excellent presentation of splendid results reported.

I agree with Dr. Overholt that it would be fine for more of our medical men to hear this presentation and at the same time I think it might be mutually helpful if the surgeon had a better understanding of medical problems.

We became interested in cystic lung disease in 1933, and since this time we have had a few lung cysts successfully treated surgically. Our first patient and a number of subsequent patients have been followed to autopsy. As a result of our autopsies, we have found cystic disease usually bilateral and frequently multiple and bilateral and not amenable to surgical removal. For this reason I wish to add a word of caution in overenthusiasm for the surgical cure of cystic lung disease.

DR. R. H. MEADE, JR., Chicago, Ill.—I should have added before I closed that since this paper was completed Dr. Kay and Dr. Hughes have increased the series to 236 lobectomies without further deaths.

I appreciate very much the remarks of the discussors. I failed to go into the question of indications for operation for bronchiectasis, which was a serious omission, but was done because I was in a hurry to get through. I don't think any of us who do this type of surgery would be willing to operate on a patient merely because there was x-ray evidence of bronchiectasis, unless it was of such extensive nature that we feared that at some later time it might cause trouble. All of our patients were operated on because they not only had bronchographic evidence of disease, but they had symptoms which had existed for varying lengths of time, sometimes for a month, sometimes for a year, symptoms which had failed to respond to conservative methods. They had repeated bronchoscopic exploration, penicillin by all routes, and all such measures as that. The question with regard to this subject was very well timed.

In regard to the extent of the disease for which we were willing to operate, we did not refuse operation to any patient who had the equivalent of two uninvolved upper lobes. If we could leave the patient with both upper lobes, he was given a chance at operative treatment.

There were many patients with evidence of bronchiectasis which we thought was of too minimal nature to warrant lobectomy. There were very few of those in this series that had too extensive disease.

As to the etiology, I am not prepared to discuss that. It is too important a question to discuss briefly. I would like to say, however, that quite a number of our patients had symptoms that did not appear prior to their service in the Army. A good many patients had symptoms going back to childhood. They obviously had had the disease for many years but it had not been sufficiently evident to keep them from being inducted.

A FOLLOW-UP STUDY OF THE CARDIOPULMONARY FUNCTION IN FOUR YOUNG INDIVIDUALS AFTER PNEUMONECTOMY

A. Cournand, M.D., A. Himmelstein, M.D., R. L. Riley, M.D., and C. W. Lester, M.D.
New York, N. Y.

SEVERAL years ago, three reports were published, providing a physiologic background for some of the clinical problems posed by the ablation of one lung.[1-3] These gave information concerning: (a) the state of respiratory gases in the arterial blood of adult patients during the immediate postoperative period; (b) the changes in lung volumes, in ventilatory and in alveolorespiratory functions, at rest and during moderate exercise, as observed in adult patients several months after operation; (c) the changes in lung volumes, and in ventilatory and alveolorespiratory functions at rest, during moderate, and during exhausting exercise in three young individuals who were still in their period of growth when studied a few years after pneumonectomy. A follow-up study of these three subjects is presented here. They have now reached late adolescence or adult age. A fourth case studied more recently has been added to this small group. Thus, information of physiologic interest is extended to a period of life which proved to be critical in the study of the late effects of pneumonectomy performed in puppies reported by Longacre and associates.[4] Since information has been secured concerning the state of the lesser circulation by making use of the technique of catheterization of the right heart, the over-all picture of the effects of pneumonectomy upon cardiopulmonary functions may now be viewed in a better perspective.

MATERIAL FOR STUDY

In these four cases, the left lung was resected during childhood, in one or in several stages, for bronchiectasis or pulmonary suppuration. Clinical histories in three of the four cases have been given elsewhere.[1] A brief summary of the most pertinent clinical data follows:

Case 1.—H. W., a white girl, was born in 1931. Tourniquet left lower lobectomy was performed in October, 1936, and tourniquet left upper lobe lobectomy in October, 1937. Thoracotomy was done in November, 1939. The stem bronchus was resected for infected pocket at the ends of open branch bronchi in April, 1940. Since 1943, the presence of a small air pocket has been noted on the left side.

Case 2.—J. L., a colored boy, was born in 1929. Tourniquet left pneumonectomy was done in November, 1939. Postoperative empyema drained and healed in March, 1940.

Case 3.—R. G., a white boy, was born in 1927. He had a tourniquet left pneumonectomy in February, 1938, and intermittent opening of a bronchopleural fistula since that time.

From the Department of Medicine, College of Physicians and Surgeons, Columbia University, the Chest Service and The Children's Surgical Service, Bellevue Hospital.
Under a grant from the Commonwealth Fund.
Read at the Twenty-sixth Annual Meeting of The American Association for Thoracic Surgery, Detroit, Mich., May 29, 30, and 31, 1946.

CASE 4.—E. B., a white girl, was born in 1926. She had a tourniquet left lower lobe lobectomy in January, 1936, for bronchectasis, individual ligation left upper lobe lobectomy in December, 1942, and limited thoracoplasty in February, 1943, for the relief of symptoms attributed to the marked displacement of the esophagus toward the operated side.

The four subjects lead a normally active life. They work and play and apparently are not limited in their physical activity.

A set of two x-rays of the chest for each case, one in deep inspiration, the other in forced expiration, is shown in Figs. 1 to 4, to demonstrate the position and the amplitude of motion of the ribs, diaphragm, and mediastinum. In Cases 1, 2, and 3, they may be compared to the sets of x-rays published in the first report.[1] It will be noted that in Cases 1 and 3 there is still no x-ray evidence of distention of the right lung as judged on the expiratory film from the position of the trachea and the heart and the absence of mediastinal hernia. A highlight in the upper half of the left chest in both of these cases suggests the presence of air. In Case 2, the x-ray shows that the right lung is still overdistended in expiration, as it was five years ago. In Case 4, there is evidence on the inspiratory and the expiratory films of two distinct mediastinal hernias of the right lung into the left chest. The amplitude of motion of the right diaphragm in these two cases is small.

In Table I are summarized the physical characteristics of the four cases at the time each series of studies was done.

TABLE I. PHYSICAL CHARACTERISTICS OF FOUR SUBJECTS AFTER LEFT PNEUMONECTOMY

SUBJECT	DATE	AGE (YR.)	HEIGHT (CM.)	WEIGHT (KG.)	BODY SURFACE AREA (M^2.)
H. W.	1940	9	133	32.5	1.08
	1943	11.5	155	37.5	1.29
	1943	12	159	40.0	1.36
	1945	13.5	161	56.0	1.58
	1946	14.5	163	60.0	1.64
J. L.	1940	11.5	158	45.5	1.43
	1943	13	172	65	1.77
	1944	15	172	65	1.77
	1945	16	172	67	1.80
	1946	18	172	66	1.78
R. G.	1940	14	163	45	1.46
	1943	16	173	54.9	1.64
	1945	19	177	57	1.71
E. B.	1942*	17	155	51.8	1.48
	1943†	18	155	51.8	1.48
	1946‡	20	155	53.5	1.52

*Study just prior to pneumonectomy after left lower lobectomy.
†After pneumonectomy.
‡After thoracoplasty.

METHOD OF STUDY

The following measurements were made repeatedly over a period of five years. The last series of measurements was obtained during the winter of 1945 to 1946.

1. Lung volume.
2. Pulmonary emptying rate.

Fig. 1.—H. W. X-ray taken at time of the most recent study. Film in deep inspiration to the left, in forced expiration to the right. Note: (1) large amplitude of motion of the diaphragm; (2) trachea in midline in expiration; (3) highlight in left hemithorax; and (4) small air sac herniating into the right lung field on forced expiration.

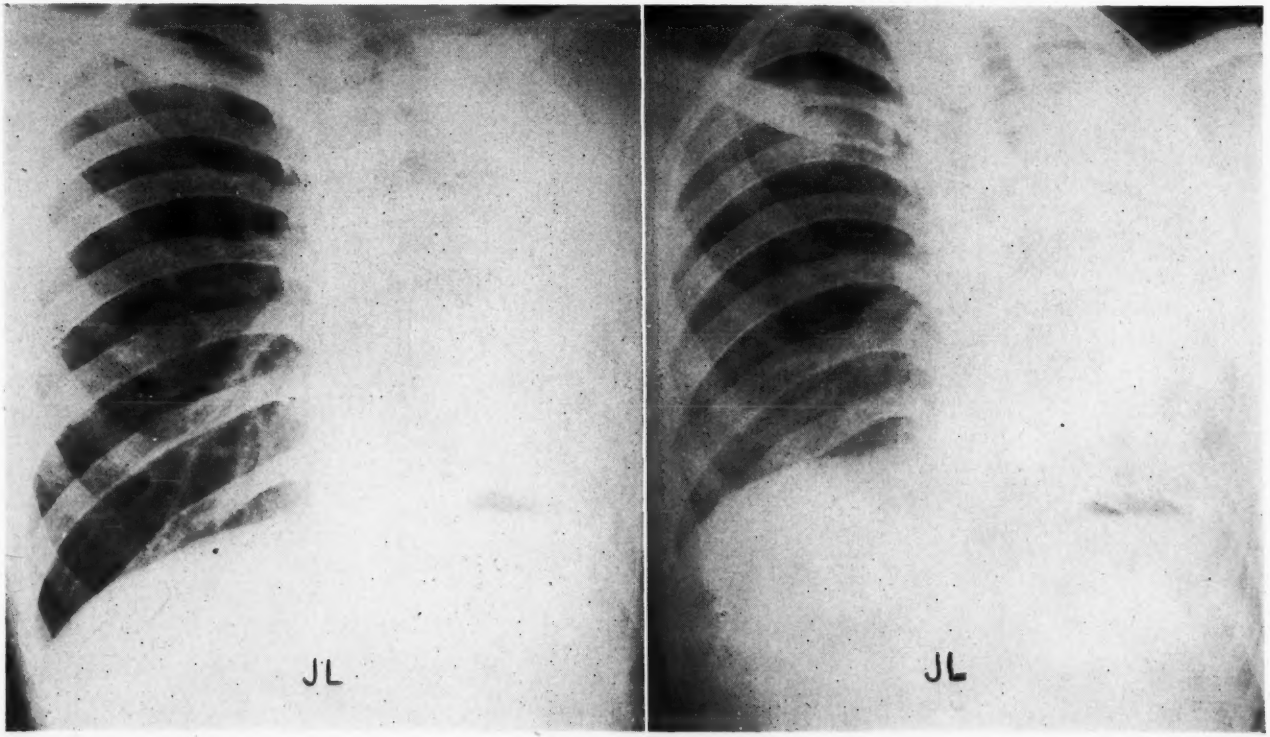

Fig. 2.—J. L. (see legend, Fig. 1.) Note: (1) small amplitude of motion of the diaphragm; (2) trachea displacement towards the left in forced expiration; and (3) posterior mediastinal hernia.

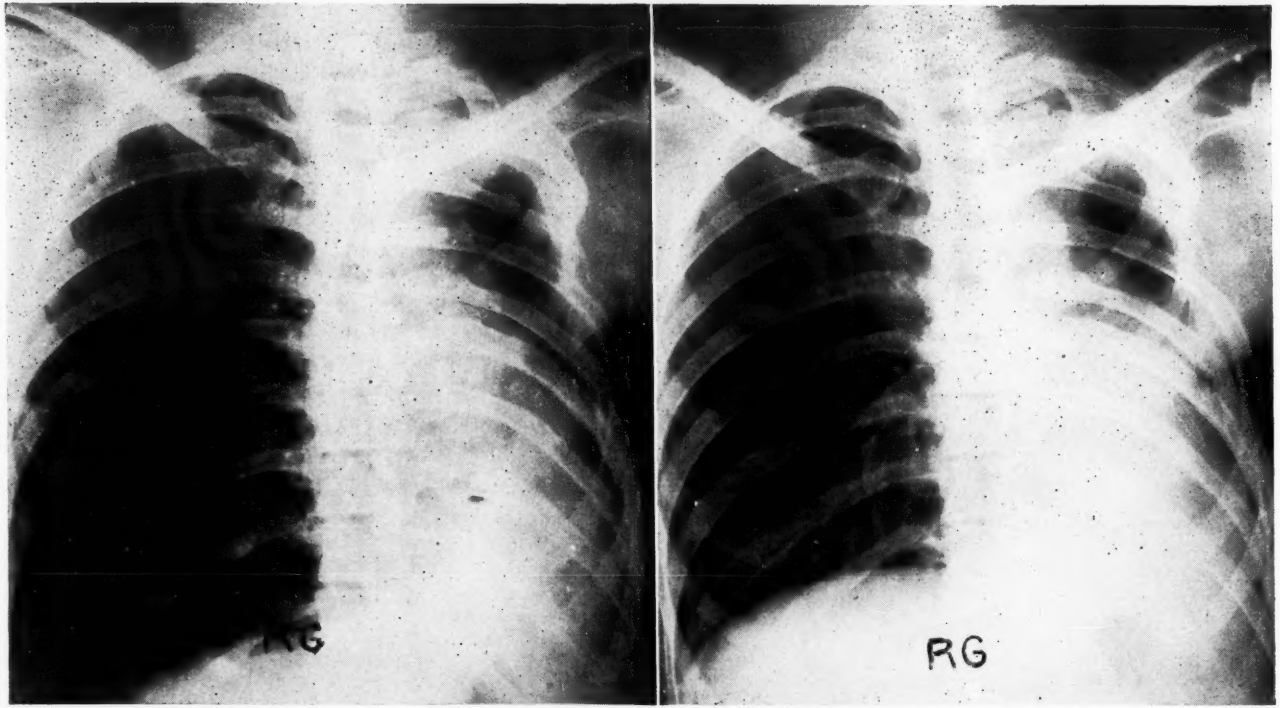

Fig. 3.—R. G. (see legend, Fig. 1.) Note: (1) large amplitude of motion of the diaphragm; (2) trachea in midline in expiration; and (3) highlight in left hemithorax.

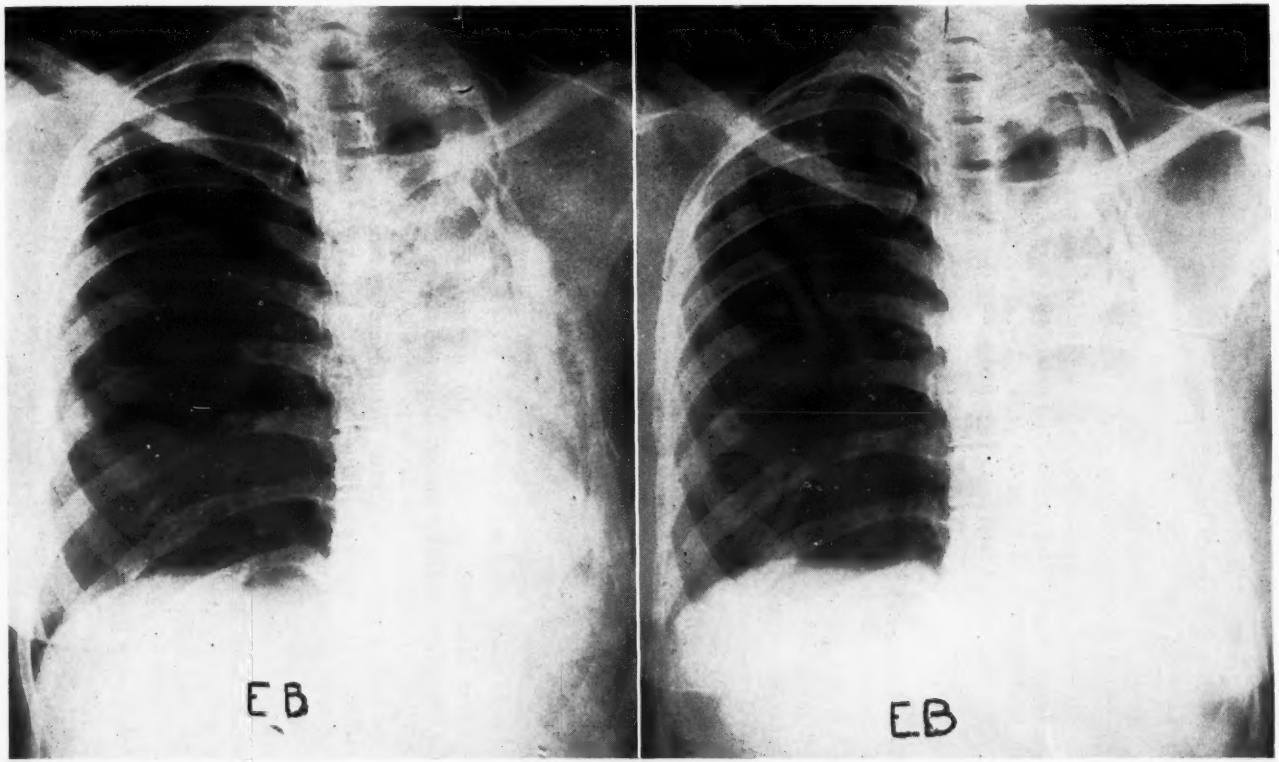

Fig. 4.—E. B. (see legend, Fig. 1.) Note: (1) small amplitude of motion of the diaphragm; (2) trachea in midline in expiration; (3) two highlights in the left hemithorax characteristic of anterosuperior and posteroinferior mediastinal hernias.

3. Maximum breathing capacity.
4. Ventilation and respiratory gas exchange under basal conditions, during and after a moderate type of exercise, and during the last minute of an exhausting type of exercise.
5. State of respiratory gases in the arterial blood, at rest, and immediately following completion of the moderate and the exhausting exercises.

At the time of the last studies, following the introduction of a catheter into the right heart by way of the venous system, records of pressures in the right ventricle, and in one instance in the pulmonary artery (Case 3), and measurements of cardiac output were obtained in three of the four cases (Cases 2, 3, and 4).

TECHNIQUES

The techniques used for the studies of pulmonary function have been described elsewhere.[1, 2, 5] A table, summarizing the various measurements, their significance and normal values, and giving bibliographical references, has been prepared previously.[2] In this report, the method for prediction of the maximum breathing capacity is based on correlation data obtained in two series of fifty normal male patients and forty normal female patients with ages ranging from 10 to 65 years.

The following regression formulas were used for the calculation of the predicted normal values:

M.B.C.* (males) L./min. = (86.5 − [.522 × age in years]) × B.S.A.†($M.^2$)
M.B.C. (females) L./min. = (71.3 − [.474 × age in years]) × B.S.A.($M.^2$)

In the first report, the normal values for a maximum breathing capacity was obtained from a very small group of controls.

Predicted normal values for lung volumes were based on age, sex, and body size, and taken from available sources in the literature[1, 6, 7] using 55 per cent of the figure for two lungs as the figure for the right lung only. As in the first report, exhausting exercise consisted in stepping up and down a small step 20 cm. high forty or more times a minute for a period up to four minutes. Control values of total oxygen intake during the last minute of this type of exercise obtained in a group of normal adolescents[1] were used for the two female subjects H. W. (Case 1) and E. B. (Case 4). The control values for the two male subjects are based on measurements of oxygen consumption made in normal subjects while running on a motor driven treadmill inclined so as to provide an 8.6 per cent uphill grade, at a rate which exhausted them in from two to five minutes.[7] The energy expenditure in this type of exercise is at least 20 per cent greater than with the step test and, therefore, these control values are probably too high for accurate comparison. Details of the technique of right heart catheterization, recording of intracardiac pressures, and measurement of cardiac output are described elsewhere.[8]

*M.B.C., maximum breathing capacity.
†B.S.A., body surface area expressed in square meters.

RESULTS

Lung Volumes.—(Table II, and Chart 1.)

Total capacity: In H. W., J. L., and R. G. (Cases 1 to 3) the total capacity of the right lung has increased during the period of growth, and in the two adult males, J. L. and R. G. (Cases 2 and 3) it has not changed significantly in the last few years. In E. B. (Case 4), there has been a slight increase in size between the second and the third study. In the four cases the volume of the right lung in maximum inspiration is greater than the predicted value for the right lung of a normal individual.

TABLE II. LUNG VOLUMES* AFTER LEFT PNEUMONECTOMY

SUBJECT	DATE	TOTAL CAPACITY (LITERS)		VITAL CAPACITY (LITERS)		RESIDUAL AIR (LITERS)		RESIDUAL AIR / TOTAL CAPACITY × 100	
		PREDICTED VALUE, RIGHT LUNG	OBSERVED	PREDICTED VALUE, RIGHT LUNG	OBSERVED	PREDICTED VALUE, RIGHT LUNG	OBSERVED	NORMAL	OBSERVED
H. W.	1940	1.30	1.61	1.04	1.30	0.27	0.29	20.4	17.9
	1943	–	–	1.32	2.12	–	–	–	–
	1943	1.93	2.62	1.54	2.16	0.39	0.47	20.4	17.4
	1945	–	–	1.97	2.78	–	–	–	–
	1946	2.51	3.46	2.00	2.80	0.51	0.66	20.4	19.1
J. L.	1940	1.57	2.16	1.25	1.58	0.32	0.58	20.4	26.7
	1943	2.32	3.20	1.85	2.43	0.47	0.77	20.4	24.0
	1944	3.15	4.07	2.49	2.73	0.66	1.51	19.8	37.2
	1945	3.15	3.98	2.49	2.57	0.66	1.41	19.8	35.4
	1946	3.15	4.12	2.49	2.70	0.66	1.42	19.8	34.5
R. G.	1940	2.32	2.94	1.85	2.47	0.47	0.47	20.4	16.0
	1943	3.18	3.68	2.58	3.21	0.60	0.47	19.8	12.8
	1945	3.35	4.12	2.68	3.42	0.67	0.70	19.8	17.0
E. B.	1942†	3.28‖	2.34	2.60‖	1.89	0.68‖	0.45	20.4	19.3
	1943‡	1.80	2.04	1.43	1.56	0.37	0.48	20.4	23.9
	1946§	2.07	2.33	1.65	1.43	0.42	0.89	20.4	38.6

*Saturated gas at 37° C. and prevailing barometric pressure.
†Study just prior to pneumonectomy after left lower lobectomy.
‡After pneumonectomy.
§After thoracoplasty.
‖Normal for both lungs.

Residual air: The absolute values for residual air have increased with age in the three subjects previously reported. In Cases 1 and 3, it is not greater than the predicted residual air volume for a normal right lung. It is more than double the predicted volume in Cases 2 and in 4. In the last case it has increased by 400 c.c. between the second and third study.

Ratio of $\frac{\textit{Residual air}}{\textit{Total lung capacity}} \times 100$*:* This ratio, which is a good index of pulmonary distention and pulmonary emphysema, was normal in Cases 1 and 3 at the time of the first studies, and with growth of the lung has remained normal. In Case 2 the ratio was high at the time of the first study, became higher in subsequent studies, but has not changed very significantly since he reached full body development. In Case 4, it has markedly increased between the second and the third study.

Vital capacity: In the three cases reported previously, the vital capacity has been larger than the predicted value both during the period of growth and since full development has been reached. In Case 4, it has decreased somewhat since pneumonectomy and is smaller than the predicted value for a normal right lung.

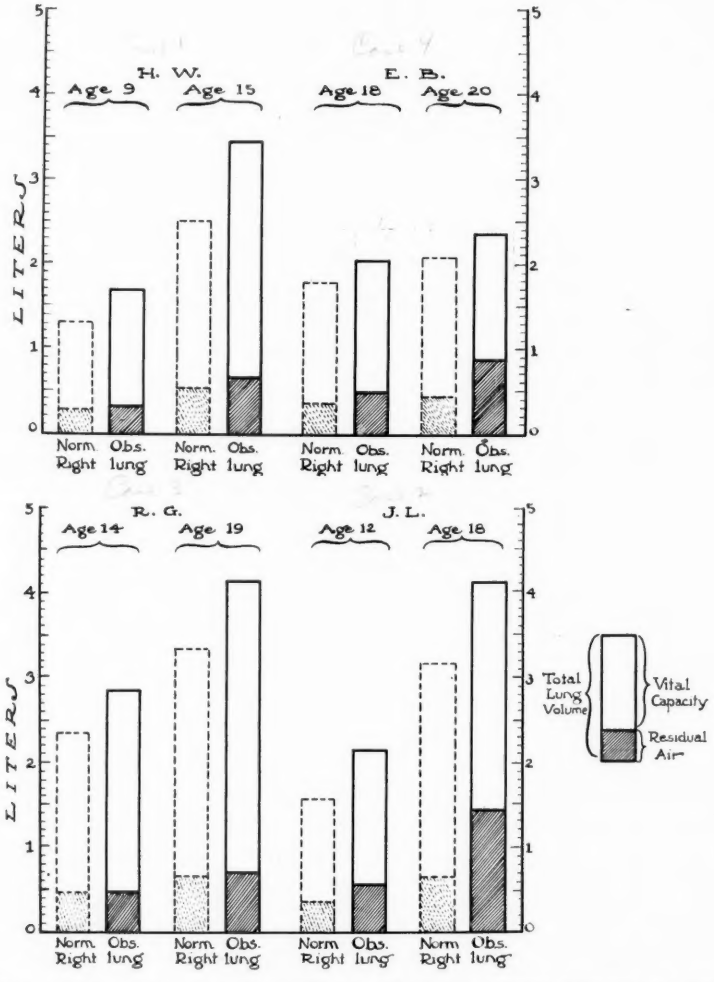

Chart 1.—Lung volumes in liters. Blocks with broken outlines represent the predicted values for the right lung of a normal subject of same size and sex at age indicated above. Blocks with solid outlines represent the observed values at the age indicated above. Key to the lung volumes subdivisions to the right.

In summary, the right lung of the three cases reported previously has grown during adolescence. In Cases 1 and 3 (H. W. and R. G.), the lung volume measurements are not indicative of pulmonary distention. The volume changes

between forced expiration and full inspiration show that the remaining lung expands more than one of a pair of normal lungs, presumably[2] because in deep inspiration there is no contralateral lung to prevent the expansion of the mediastinal part of the remaining lung into the opposite chest. In Case 2 (J. L.), distention of the right lung present five years ago has persisted but apparently has not increased in the last three years. In Case 4 (E. B.), the right lung has become distended within three years after a pneumonectomy and a limited thoracoplasty. As yet, there is no data to show whether or not the distention is increasing.

These data confirm and amplify the information obtained from the study of the x-ray films taken in deep inspiration and forced expiration (Figs. 1 to 4).

Pulmonary Emptying Rate.—(Table III.) Under this heading may be described a test in which the alveolar nitrogen concentration is measured in alveolar samples taken after seven minutes of pure oxygen breathing.[11] In this procedure, the rate of displacement of nitrogen by oxygen depends upon four factors: (a) the relative volume of tidal air and functional residual air; (b) the size of the anatomic dead space, which does not contribute to gas exchanges (tracheabronchi-bronchioles); (c) the mode of distribution of the tidal air into the alveolar spaces; (d) the rate of nitrogen diffusion from the capillaries into the alveoli as the oxygen concentration increases. In all but one of the studies, the alveolar nitrogen concentration at the end of seven minutes of pure oxygen breathing was well below 2 per cent, the upper limit of normal.

TABLE III. PULMONARY EMPTYING RATE AFTER LEFT PNEUMONECTOMY

SUBJECT	DATE	FUNCTIONAL RESIDUAL AIR VOLUME* (C.C.)	AVERAGE TIDAL AIR VOLUME* (C.C.)	AVERAGE RESPIRATORY RATE (PER MIN.)	ALVEOLAR N_2 AFTER SEVEN MINUTES O_2 BREATHING	
					OBSERVED (%)	CALCULATED† (%)
H. W.	1940	550	–	–	0.59	–
	1943	1000	–	–	0.95	–
	1946	1200	483	14.3	0.93	1.12
J. L.	1940	1010	–	–	0.77	–
	1943	1440	–	–	1.43	–
	1944	2310	–	–	1.20	–
	1945	1970	463	21.6	1.53	0.99
	1946	2020	–	–	1.17	–
R. G.	1940	1140	–	–	0.99	–
	1943	1450	–	–	1.04	–
	1945	1570	476	21.2	1.20	0.97
E. B.	1942	840‡	–	–	1.39	–
	1943	780§	–	–	2.19	–
	1946	1180	371	16.3	1.15	1.16

*Saturated gas at 37° C. at prevailing barometric pressure.
†Formula A.[11]
‡Before pneumonectomy, after left lower lobectomy.
§Before thoracoplasty.

This finding is not surprising in view of the fact that resection of one lung results in a diminution of the anatomic dead space by elimination of one bronchial tree, and a relative increase of the tidal air with regard to the functional residual air.

Using one set of figures for each subject, as seen in Table III, calculations were made according to a formula previously reported (formula A[11]), to determine whether the observed alveolar concentration after seven minutes of pure oxygen breathing was greatly different from the calculated value. The anatomic dead space values, indispensable in the calculation, were assumed to be 140 c.c. in the two males and 120 c.c. in the two females, and the figures of nitrogen excretion per minute were based on body size.[9] The calculated alveolar nitrogen concentration in Cases 1 to 4 were, respectively, 1.12 per cent, 0.99 per cent, 0.97 per cent, and 1.16 per cent, while the observed values were, respectively, 0.93, per cent, 1.53 per cent, 1.20 per cent, and 1.15 per cent. These figures strongly suggest that at rest the ventilation of the various parts of the lung was equal even in the cases which showed lung distention.

TABLE IV. MAXIMUM BREATHING CAPACITY, VENTILATION, AND BREATHING RESERVE DURING LAST MINUTE OF AN EXHAUSTING EXERCISE

SUBJECT	DATE	MAXIMUM BREATHING CAPACITY* (L. PER MIN.) NORMAL	MAXIMUM BREATHING CAPACITY* (L. PER MIN.) OBSERVED	VENTILATION DURING LAST MINUTE* (L. PER MIN.)	RATIO OF BREATHING RESERVE / MAXIMUM BREATH CAPACITY DURING LAST MINUTE × 100	TOTAL NO. STEPS	DURATION (MIN.)
H. W.	1940	72.5	40.5	31.7	21	160	4
	1943	85	50.8	39.7	22	170	4
	1943	89	64.3	–	–	–	–
	1945	102	72.8	–	–	–	–
	1946	105	87.0	47.4	45.5	147	3.5
J. L.	1940	115	54.6	39.4	24	138	3
	1943	141	67.2	–	–	–	–
	1944	139	65.0	–	–	–	–
	1945	141	65.0	–	–	–	–
	1946	136	74.8	49.0	34.6	85	2
R. G.	1940	115	86.3	44.0	45.8	150	4
	1943	128	102.9	–	–	–	–
	1945	137	102.5	60.5	41	146	3
E. B.	1942†	90	64.3	–	–	–	–
	1943‡	92	59.4	–	–	–	–
	1946§	94	51.3	41.2	19.7	114	3

*Saturated gas at 37° C. and prevailing barometric pressure.
†Before pneumonectomy after left lower lobectomy.
‡After pneumonectomy.
§After thoracoplasty.

Ventilatory Function.—

Maximum breathing capacity: (Table IV and Chart 2.)

In Cases 1 and 3, the maximum breathing capacity increased during the period of growth, and is at present 83 per cent and 75 per cent of normal, respectively. In Case 2, the maximum breathing capacity increased somewhat less during the period of growth, and is now only 55 per cent of normal. In Case 4, the maximum breathing capacity decreased between the second and the third study to a value which is 55 per cent of normal.

These findings are consistent with the repeated observation that when the ratio of $\frac{\text{residual air}}{\text{total lung capacity}} \times 100$ increases (when the lungs become distended

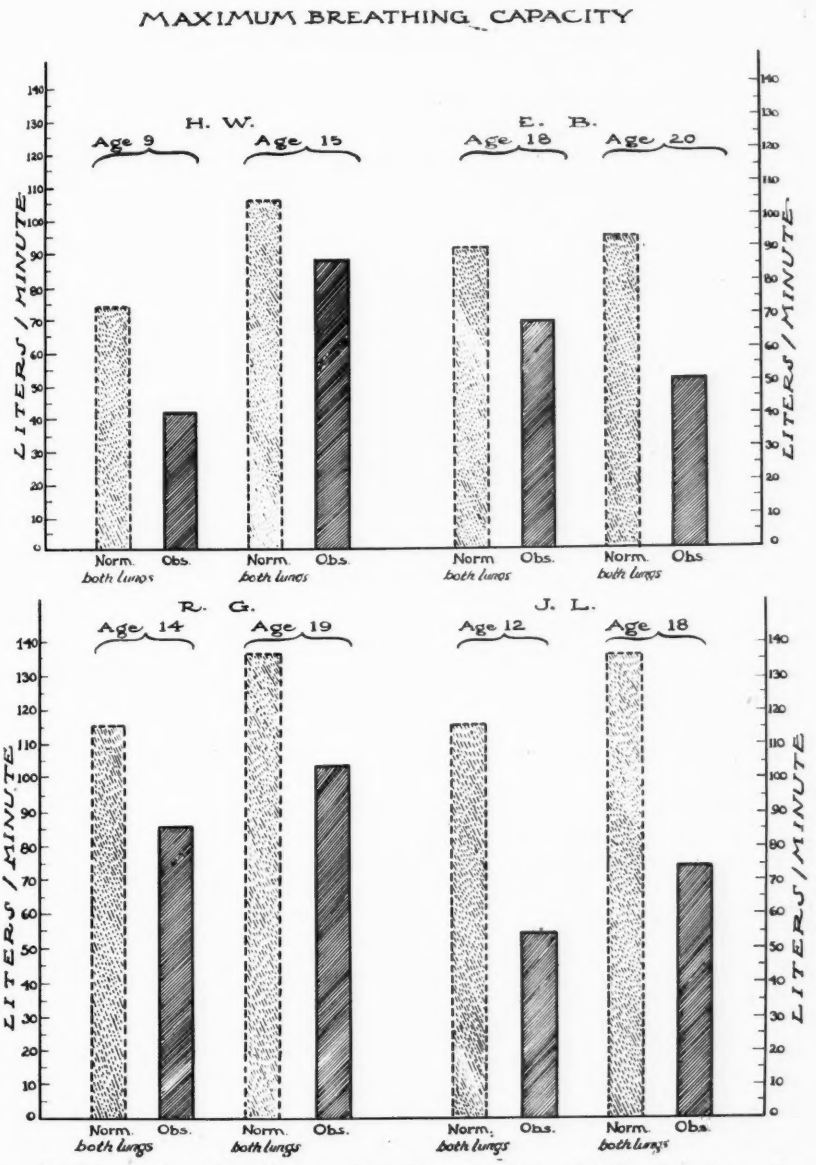

Chart 2.—Maximum breathing capacity in liters per minute. Blocks with broken outlines represent the predicted values in a normal individual of the same size and sex at age indicated above. Blocks with the solid outlines represent the observed values at the age indicated above.

or emphysematous), the ventilatory efficiency of the chest bellows decreases. Therefore, it is not surprising that the maximum breathing capacity should be relatively smaller in cases with pulmonary distention than in those without distention.

Ventilation and breathing reserve during an exhausting exercise: (Table IV and Chart 3.) Data on ventilation at rest, during moderate exercise, and during the five-minute period of recovery from moderate exercise, obtained in some of the follow-up studies, have been omitted from this report, since they failed to show any significant variation from normal values.

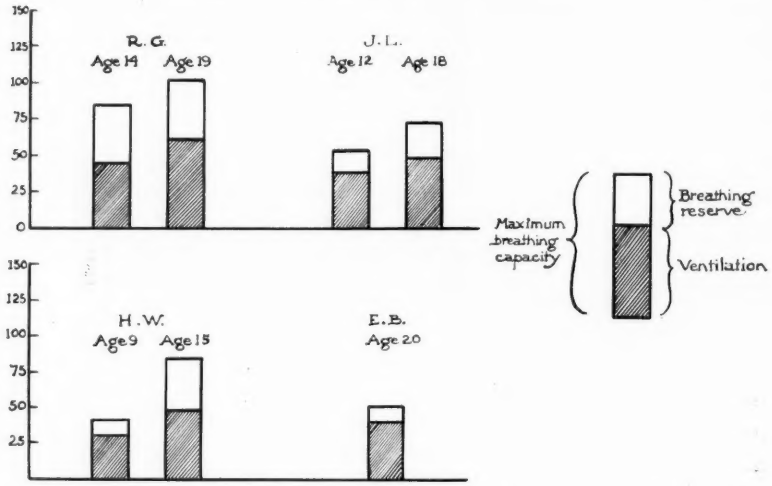

Chart 3.—Ventilation and breathing reserve during last minute of exhausting exercise.

In the recent series of studies, the breathing reserve during the last minute of the exhausting exercise was much smaller in the cases with pulmonary distention than in the cases without distention. The low ratio of $\frac{\text{breathing reserve}}{\text{maximum breathing capacity}} \times 100$ in Cases 2 and 4 was due to a low maximum breathing capacity rather than to a relatively large increase in ventilation. The duration of dyspnea in these two cases after the end of exercise was much larger than in Cases 1 and 3. This is in accord with the general trend relating the ratio of $\frac{\text{breathing reserve}}{\text{maximum breathing capacity}} \times 100$ with the severity of dyspnea.[5] Table IV shows, in addition, that the amount of work performed by J. L. and E. B. (Cases 2 and 4) on the basis of number of steps and duration of exercise was much less than in Cases 1 and 3. The probable causes of this poorer performance will be discussed later.

In summary, the maximal ventilatory capacity of the chest bellows in the subjects with pulmonary distention was smaller than in the subjects without pulmonary distention.

Alveolorespiratory Function.—

Respiratory gas exchange during the last minute of an exhausting exercise: (Table V.) No significant change from normal was found in carbon-dioxide output and oxygen intake at rest, during moderate exercise, and during the following five minutes of recovery. The data, therefore, are omitted.

In the most recent studies on the two female subjects, the oxygen intake during the last minute of the exhausting exercise was 17 per cent lower than the predicted value. From the initial to the last study, on the two male subjects, there was a progressive increase in oxygen consumption per unit of body size. In the most recent study on Case 3, the oxygen consumption during the third minute of exercise was 19 per cent below the control value, still within the range of normal variation. In the comparable study of Case 2, the oxygen consumption during the second and last minute of exercise was lower than in Case 3.

TABLE V. OXYGEN CONSUMPTION AND RESPIRATORY QUOTIENT DURING LAST MINUTE OF EXHAUSTING EXERCISE

		OXYGEN INTAKE PER MINUTE*					
SUBJECT	DATE	NORMAL (C.C. PER M.² BODY SURFACE)	OBSERVED (C.C. PER M.² BODY SURFACE)	NORMAL (C.C. PER KG.)	OBSERVED (C.C. PER KG.)	OBSERVED (C.C. PER L. OF VENTILATION)	RESPIRATORY QUOTIENT
H. W.	1940	955†	1043	32.5†	34.8	42.2	.93
	1943	1050†	1167	34.0†	40.0	44.4	.86
	1946	1370‡	1135	41.5‡	31.0	46.1	.99
J. L.	1940	1145†	1190	34.6†	35.7	49.5	1.05
	1946	2120‡	1575	53.0‡	42.5	60.0	.88
R. G.	1940	1370†	1217	41.5†	37.4	46.1	1.03
	1945	2120‡	1705	53.0‡	51.1	55.9	.90
E. B.	1946	1370‡	1136	41.5‡	31.7	48.7	.94

*Dry gas at 0° C. and 760 mm. Hg.
†From Lester, Cournand, and Riley.[1]
‡From Robinson, for males.[7]

TABLE VI. ARTERIAL OXYGEN SATURATION AFTER PNEUMONECTOMY IN BASAL STATE, IN EARLY RECOVERY FROM MODERATE EXERCISE, AND IN EARLY RECOVERY FROM EXHAUSTING EXERCISE

		OXYHEMOGLOBIN SATURATION			
			EARLY RECOVERY		
SUBJECT	DATE	BASAL (%)	MODERATE EXERCISE (%)	EXHAUSTING EXERCISE (%)	TOTAL HEMOGLOBIN (GM.)
H. W.	1940	95.7	97.8	98.0	13.3
	1943	97.5	96.4	–	12.5
	1946	–	–	92.0	–
J. L.	1940	95.3	–	92.4	13.0
	1946	96.2	–	82.5	13.8
R. G.	1940	92.6	92.8	96.6	13.4
	1943	–	–	–	14.7
	1945	98.8	95.4	92.9	14.5
E. B.	1946	97.0	98.8	83.6	13.6

State of Respiratory Gases in the Arterial Blood.—(Table VI.) In all studies of patients at rest and after moderate exercise, the figures for arterial blood oxygen saturation were within the normal range of variation. Important changes with regard to oxygenation of the blood immediately following exhausting exercise were observed during the most recent studies in Cases 2 and 4. In these two cases with pulmonary distention, the arterial blood saturation, measured immediately after the end of the exhausting exercise, was at the low level of 83 per cent and 84 per cent, respectively, whereas in Cases 1 and 3, without distention it was 92 per cent and 93 per cent, respectively. It may be argued that the poorer performance of Case 4, and especially of Case 2 during the exhausting exercise was related to the marked anoxia which caused rapid muscular fatigue and blunting of mental stimulus to carry on the task.

Dynamics of the Lesser Circulation.—(Table VII.) Information concerning the effects of pneumonectomy upon the lesser circulation were obtained by measuring the blood pressure in the right ventricle in Cases 2, 3, and 4, and in the pulmonary artery of Case 3.

TABLE VII. HEMODYNAMICS AFTER LEFT PNEUMONECTOMY

SUBJECT	DATE	RIGHT VENTRICULAR PRESSURE		PULMONARY ARTERY PRESSURES	ARTERIAL PRESSURE	CARDIAC OUTPUT	PULSE RATE
		SYST./DIAST. MM. HG	PULSE PRESSURE	SYST./DIAST. MM. HG	SYST./DIAST. MM. HG	(L. PER M.^{2} PER MIN.)	
J. L.	1946	27/0	27	–	130/81	2.94	70
R. G.	1945	31/3	28	32/9	–	3.26	90
E. B.	1946	33/3	30	–	130/78	4.80	96

The systolic and pulse pressures in the right ventricle were at the upper level of normal,[10] indicating that no significant degree of hypertension in the lesser circulation necessarily develops in the young adults or adolescents several years after the pulmonary vascular bed has been reduced in size by one-half. The finding is of special significance as these subjects were never limited in their physical activity since control of their suppurative disease. In Case 3, both systolic and diastolic pressures in the pulmonary artery were normal. In three cases, the figures for cardiac output, measured under basal conditions, indicate that the total blood flow through one lung was approximately the same as that of the normal blood flow through two lungs.

DISCUSSION

The data secured in this small group provides useful information concerning the physiologic effects of the resection of one lung on: (a) the ventilatory capacity of the chest bellows; (b) the efficiency of alveolar ventilation and of oxygen transport across the alveolocapillary membrane at various levels of physical activity; and (c) the flow and pressure adjustments in the lesser circulation.

1. The viewpoint many times expressed, that the changes in the ventilatory capacity of the chest bellows are not closely correlated with changes in lung volumes, is confirmed. If the resection of one lung is not complicated by distention of the remaining lung, figures for maximum breathing capacity compare

well with figures obtained in normal individuals. When pulmonary distention develops, the reduction is always significant and grossly proportional to the increase in the ratio of $\frac{\text{residual air}}{\text{total lung volume}} \times 100$.

2. During quiet breathing in young adults after pneumonectomy, the efficienty of alveolar ventilation is apparently maintained at a normal level. Even in patients who develop a moderate degree of pulmonary distention with or without mediastinal hernia, the study of the pulmonary emptying rate indicates that there is no significant increase in the ventilatory dead space with corresponding decrease in the volume of effective tidal air, and that the intrapulmonary mixture of respiratory gas during quiet breathing is nearly perfect, i.e., the distribution of the effective tidal air (tidal air minus dead space) is homogenous throughout the entire alveolar space. These findings confirm the statement made previously[2] that, after resection of one lung, a higher ratio of tidal air to functional residual air and a better expansion of the mediastinal portion of the lung toward the opposite hemithorax favor efficient and homogenous alveolar ventilation.

Using an original technique for the study of the efficiency of alveolar ventilation, Birath[12] reports on two patients, aged 44 and 53, several years after pneumonectomy. He concludes tentatively that this function was "generally reduced in comparison with the normal, but no very considerable impairment occurred." In both instances pulmonary distention of the remaining lung was present. Information from a larger series is necessary, since the problem of efficiency of alveolar ventilation after pneumonectomy in the older age group frequently is complicated by the presence of a preexisting moderate degree of pulmonary emphysema.

As judged from the level of oxygen saturation in the arterial blood, at rest and following moderate exercise, the efficiency of oxygen transport across the alveolocapillary membrane was normal even in the two subjects with pulmonary distention. The results, however, were quite different during the performance of an exhausting exercise, and justify some comments.

Recently published data[13] gives information on normal subjects concerning the intimate mechanism of oxygen transport across the alveolocapillary membrane at rest and during a strenuous type of exercise. These form a good basis for comparison with the small group reported. Using a new technique for the determination of the oxygen pressure (pO_2) in the alveoli and in the arterial blood, Lilienthal and Riley[13] in one normal subject found that while the oxygen consumption during the last minute of exercise increased twelvefold over the resting value, the alveolo-arterial pO_2 difference rose from 11 to 35 mm. Hg.; the alveolar pO_2 increased slightly during exercise, while the arterial pO_2 dropped from 95 to 74 mm. Hg. This latter value plotted on an oxygen dissociation curve corresponds approximately to a 92 per cent oxygen saturation. The response of one of our subjects (Case 3), to a strenuous exercise was quite similar. In this case the oxygen consumption during the last minute of the exercise increased twelvefold over the resting value, and the oxygen saturation in the arterial blood dropped to 93 per cent. In the normal subject studied by Lilienthal

and Riley as well as in Case 3, the same relative increase in oxygen transport across the alveolar capillary membrane, corresponding to an identical increase in the alveolo-arterial pO_2 difference, would require an equivalent increase in the volume of blood exposed to alveolar air (a fourfold increase in the oxygen diffusion constant of the lung).[14] It is a matter for speculation whether this increase was due, in the same balanced fashion, to an acceleration in blood flow,[15] an increase in capillary blood volume[15] due to opening of new alveolocapillary units, opening of additional capillaries in existing alveoli, or increase in the cross-section area of the existing capillaries. In both subjects with pulmonary distention, the arterial oxygen saturation fell to 83 per cent; this value corresponds to an arterial pO_2 of approximately 50 mm. Hg. This low value could be associated with the maintenance of a normal alveolocapillary pO_2 gradient, concomitant with a very considerable reduction in alveolar pO_2 due to inefficient alveolar ventilation, or a considerable increase in alveoloarterial pO_2 difference due to insufficient acceleration of the blood flow and/or inadequate increase in pulmonary capillary blood volume. In view of the high values of oxygen consumption observed during the last minute of exercise in both these cases, it would seem that inefficient ventilation of alveoli still actively perfused is the more likely cause of the reduction in arterial blood saturation.

3. It is well known from experimental studies on dogs[16, 17] that the capacity of the small pulmonary vessels is such that a several fold increase in blood flow may be accommodated with negligible pressure changes. With a safe method now available for recording pressures in the right heart and for measuring the pulmonary blood flow, it has been possible to extend to man observations on the dynamic adjustments of the lesser circulation to a large reduction in the size of the pulmonary vascular bed. A study is in progress[18] covering a variety of conditions resulting in such a reduction. Thus far, eighteen subjects have been studied, including four cases of fibrothorax, eight cases of pneumothorax, three cases of pneumonectomy performed in older age subjects, in addition to the three cases reported here. In only one case was there definite evidence of lesser circulation hypertension. This was in a man, 69 years old, whose left lung had been resected six years previously for carcinoma of the left main bronchus, and who, preoperatively, had been shown to have developed chronic pulmonary emphysema.[2]

In individuals with only one lung, preservation of normal pressure-flow relationship may be achieved in two ways which may complement each other: (a) by an increase in the number of capillaries, or (b) by an increase in their size. By a simple calculation, based on Poiseuille's law, it can be shown that an increase of only 16 per cent of the diameter of the capillaries of one lung would allow for a 100 per cent increase in pulmonary blood flow to occur without any change in pressure in the pulmonary artery.

Considering now the anatomic adjustments following pneumonectomy in growing subjects, it is noted that pulmonary distention has developed in only two out of the four subjects reported. Pulmonary distention after pneumonectomy does not appear to be a compensating process. It depends strictly upon the prevailing mechanical condition, among which the flexibility of, and the

presence of weak points in the mediastinum stand foremost. In this respect growing individuals and adults are not different from growing puppies or adult dogs. The chief difference has been, in contrast to what happens in dogs[4] and in some adult subjects, that distention remained moderate. It increased somewhat in one case while the lung grew, but has ceased to increase in the last three years. It is unlikely that this moderate degree of distention will ever lead to pulmonary emphysema. In contrast to what is seen in pulmonary emphysema, the disability that it causes was brought out only by a very strenuous exercise. Hence, attempts at correcting pulmonary distention or reducing the mediastinal hernias by an extensive resection of the chest wall would not appear indicated at this time. Whether some measures should be taken early after pneumonectomy in children to limit or prevent distention and mediastinal herniation of the remaining lung, is a matter of debate. In an attempt at maintaining the mediastinal structures in their normal position after resecton of one lung, the alternative to thoracoplasty, which in children is crippling, anatomically and physiologically,[19] would be to introduce air or oil in the hemithorax on the side of the pneumonectomy. In adults the problem is simpler, since it has been shown that an extensive thoracoplasty following pneumonectomy[2] not only does not impair the ventilation efficiency of the chest bellows, but often improves it by reducing the degree of pulmonary distention.

SUMMARY

1. The cardiopulmonary function of four patients with pneumonectomy performed during childhood or early adolescence has been followed through the period of growth.

2. The method used consisted in the study at regular intervals of the lung volumes, the ventilatory efficiency of the chest bellows, the efficiency of alveolar ventilation, and the state of respiratory gas exchanges in the lung and in the arterial blood, at rest and during a moderate and an exhausting type of exercise. At the time of the most recent study, the right ventricular pressures and the pulmonary blood flow were measured in three of the four subjects under basal conditions.

3. In two patients who developed a moderate degree of pulmonary distention, the only significant findings were a reduction in breathing reserve from normal and a marked degree of oxygen unsaturation in the arterial blood, brought out by a very strenuous type of exercise.

4. The moderate degree of pulmonary distention, which increased slightly in one subject during the period of growth of his lung, has not progressed during the last three years.

5. Performance of one subject who did not show any evidence of pulmonary distention was indistinguishable from that of a normal individual under the same strenuous circumstances.

6. No significant degree of hypertension in the lesser circulation has developed as yet.

Grateful acknowledgment for technical assistance is made to M. S. Lester, M. V. C. Jones, and B. Spierto.

REFERENCES

1. Lester, C. W., Cournand, A., and Riley, R. L.: Pulmonary Function After Pneumonectomy in Children, J. THORACIC SURG. **11**: 529, 1942.
2. Cournand, A., and Berry, F. B.: The Effect of Pneumonectomy Upon Cardiopulmonary Function in Adult Patients, Ann. Surg. **116**: 532, 1942.
3. Maier, H. C., and Cournand, A.: Studies of the Arterial Oxygen Saturation in the Postoperative Period After Pulmonary Resection, Surgery **13**: 199, 1943.
4. Longacre, J. J., Carter, B. N., and Quill, L. McG.: An Experimental Study of Some of the Physiological Changes Following Total Pneumonectomy, J. THORACIC SURG. **6**: 237, 1937.
   Carter, B. N., Longacre, J. J., and Quill, L. McG.: A Study of the Changes in Cardiorespiratory Physiology Following Total Pneumonectomy in Young Developing Animals, J. THORACIC SURG. **7**: 326, 1938.
   Longacre, J. J., and Johansmann, R.: An Experimental Study of the Fate of the Remaining Lung Following Total Pneumonectomy, J. THORACIC SURG. **10**: 131, 1940.
5. Cournand, A., and Richards, D. W., Jr.: Pulmonary Insufficiency. I-II. The Effects of Various Types of Collapse Therapy Upon Cardiopulmonary Function, Am. Rev. Tuberc. **44**: 123, 1941.
6. Kaltreider, N. L., Fray, W. W., and Hyde, H. W.: Effect of Age on Pulmonary Capacity and Its Subdivisions, Am. Rev. Tuberc. **37**: 662, 1938.
7. Robinson, Sid: Experimental Studies of Physical Fitness in Relation to Age, Arbeitsphysiology **10**: 3, 1938.
8. Cournand, A., and Ranges, H. A.: Catheterization of Right Auricle in Man, Proc. Soc. Exper. Biol. & Med. **46**: 462, 1941.
   Cournand, A., Lauson, H. D., Bloomfield, R. A., Breed, E. S., and Baldwin, E. De F.: Recording of Right Heart Pressures in Man, Proc. Soc. Exper. Biol. & Med. **55**: 34, 1944.
   Cournand, A., Riley, R. L., Breed, E. S., Baldwin, E. De F., and Richards, D. W., Jr.: Measurement of Cardiac Output in Man Using the Technique of Catheterization of the Right Auricle and Ventricle, J. Clin. Investigation **24**: 106, 1945.
   Cournand, A.: Measurement of the Cardiac Output in Man Using the Right Heart Catheterization, Federation Proceedings **4**: 207, 1945.
9. Cournand, A., Yarmush, I. V., and Riley, R. L.: Influence of Body Size on Gaseous Nitrogen Elimination During High Oxygen Breathing, Proc. Soc. Exper. Biol. & Med. **48**: 280, 1941.
10. Bloomfield, R. A., Lauson, H. D., Cournand, A., Breed, E. S., and Richards, D. W., Jr.: Recording of Right Heart Pressures in Normal Subjects and in Patients With Chronic Pulmonary Disease and Various Types of Cardio-circulatory Disease, J. Clin. Investigation **25**: 639, 1946.
11. Darling, R. C., Cournand, A., and Richards, D. W., Jr.: Studies on Intrapulmonary Mixture of Gases. V. Forms of Inadequate Ventilation in Normal and Emphysematous Lungs Analyzed by Means of Breathing Pure Oxygen, J. Clin. Investigation **23**: 55, 1944.
12. Birath, G.: Lung Volume and Ventilation Efficiency, Acta Medica Scandinavica, Supplement, 1944.
13. Lilienthal, J. L., and Riley, R. L.: An Experimental Analysis in Man of the Oxygen Pressure Gradient From Alveolar Air to Arterial Blood During Rest and Exercise at Sea Level and at Altitude, Am. J. Physiol. **147**: 199, 1946.
14. Krogh, M. J.: The Diffusion of Gases Through the Lungs of Man, J. Physiol. **49**: 271, 1915.
15. Roughton, F. J. W.: The Average Time Spent by the Blood in the Human Lung Capillary and Its Relation to the Rate of CO Uptake and Elimination in Man, Am. J. Physiol. **143**: 64, 1945.
16. Wiggers, C. J.: The Regulation of the Pulmonary Circulation, Physiol. Rev. **1**: 239, 1921.
17. Drinker, C. K., Churchill, E. D., and Ferry, K. N.: The Volume of Blood in the Heart and Lungs, Am. J. Physiol. **77**: 590, 1926.
18. Cournand, A.: Dynamics of the Lesser Circulation, Bulletin of the New York Academy of Medicine **23**: 27, 1947.
19. Cournand, A., Richards, D. W., Jr., and Maier, H. C.: Pulmonary Insufficiency. III. Cases Demonstrating Advanced Cardio-pulmonary Insufficiency Following Artificial Pneumothorax and Thoracoplasty, Am. Rev. Tuberc. **54**: 272, 1941.

DISCUSSION

DR. EDGAR W. DAVIS, Washington, D. C.—I congratulate Drs. Cournand and Lester on the preparation and presentation of their paper. Studies in surgical technique are great

contributions to thoracic surgery, but if we are to base the management of these conditions upon physiologic considerations, we must make more studies in physiology along the same lines which have been presented by Dr. Lester. I shall not discuss this paper, but shall make a few remarks which I hope will stimulate a greater interest among more men to do further work in physiology.

I think it was Dr. Longacre of Cincinnati, Ohio, who presented a paper to this association several years ago on the compensatory emphysema which developed in pneumonectomized animals. His studies showed by actual measurements that the air sac became larger in the remaining lung. This enlargement of the air sacs, which we now designate as a compensatory emphysema, is a known fact. However, the clinical significance of this compensatory emphysema in subsequent years, and the relation it will have upon the physiologic exchange of gas, are not clearly understood.

In an attempt to answer some of these questions, or at least to get a better idea about them, we have started some studies in physiology which are very interesting. Whether the results of these studies, to be published later, are of practical value, remains to be seen.

This study was prompted by the economic factor involved in the case of a patient of mine, a white man, aged 42 years, whose right lung we had removed a short time previously for bronchogenic carcinoma. He was a pilot, a captain in the Pennsylvania Central Airlines Corporation. His salary as a pilot was possibly $8,000 or $10,000 annually, whereas if he were to be reduced from a flying status to ground work, his salary would be reduced greatly. Because of this, the patient agreed to have any test which would enable us to say whether or not he could return to work as a pilot.

Dr. Ludwig Lederer, Chief of the Medical Department of the Pennsylvania Central Airlines, was very interested in the contemplated studies. It was through Dr. Lederer that the airline agreed to share with me the expense of the tests, which, to date, have been done by Dr. Ivy of Northwestern University, Chicago.

This patient and another man who served as a control were placed in a pressure chamber. Recordings were made of barometric and oxymetric readings and the temperature, pulse, and respiration of the patient and the control. Samples of their handwriting were made, hearing and interpretation of voices over the intercommunicating system were recorded, and oxygen concentrations of the arterial blood were done. These and many other studies, including x-rays of the chest, were made at ground level and at various altitudes.

It was interesting to note that the patient, as compared with the control, stood his test almost normally until an altitude of about 18,000 feet was reached. The first thing the patient noticed which was abnormal, was slight difficulty in the interpretation of voice sounds over the telephone, which occurred at an altitude of about 10,000 to 12,000 feet. The patient volunteered the information that this difficulty in understanding conversation over the intercommunicating system was extremely slight and in all probability would not have been noticed by a person unaccustomed to piloting a plane.

Another patient, 62 years of age, has been studied in a similar manner, three months following a segmental resection of the right middle lobe. We expect to carry out the same studies and possibly add others, on another series of patients of varying ages, following pneumonectomy, lobectomy, or segmental resection.

In discussing the use of lobectomy for children, we have had a small series of eighteen or twenty cases and have been very favorably impressed with the rapidity with which the restitutional processes take place.

I give you these remarks without any comment as to their practical value. It is necessary to study more patients over a long period of time before we understand the physiology as well as the anatomy of restitutional processes following resection or removal of lung tissue. My only hope is that some of you who are affiliated with teaching institutions and who have access to a good laboratory of physiology will be stimulated to pursue this work further.

THE USE OF CURARE IN ANESTHESIA FOR THORACIC SURGERY

H. Brodie Stephens, M.D., P. Harroun, M.D., and F. E. Beckert, M.D.
San Francisco, Calif.

THE high frequency cautery unit has been of great assistance in surgery for many years, decreasing blood loss and shortening the time required for operation. Surgeons working inside the pleural cavity were denied the advantages the cautery unit affords when of necessity an explosive anesthetic agent was required to provide sufficient control of the patient. Chloroform is the only nonexplosive inhalation agent potent enough to produce the apnea necessary for the use of "controlled respiration." It is the opinion of most anesthetists, however, that the toxicity of chloroform contraindicates its use in major intrathoracic operations because of their time-consuming character. Spinal analgesia has proved satisfactory in certain institutions, but many surgeons hesitate to use this technique because of the high level of analgesia that must be attained and the necessity of limiting the operating time.

The problem of combining controlled respiration with the safe use of the cautery inside the pleural cavity has been solved at the University of California Hospital by using anesthesia with nonexplosive nitrous oxide and producing apnea by the intravenous administration of curare. The technique was developed on a series of dogs and has now been used on seventy-five patients undergoing, in most instances, intrathoracic operations. These cases will be reported later in the manuscript.

Curare has been known to science since Sir Walter Raleigh[1] brought back the first arrows poisoned with this substance when he returned to England from Guiana in 1595. The supply of the drug was very limited, and it remained almost unknown until Claude Bernard,[2] working from 1857 to 1864, did the first experimental work on the material. The efforts of this investigator and his contemporaries established these facts about curare by 1865: it is a substance which paralyzes voluntary muscle by breaking the connection between muscle and motor nerve, it kills by respiratory paralysis, and it does not produce analgesia. These facts represent practically all that is known positively about the drug to this day, and even now the last statement is disputed by some anesthetists.

Curare was used intermittently during the late nineteenth and early twentieth centuries for various diseases where muscular relaxation was needed. Rabies, tetanus, and epileptiform seizures represent the main group of diseases where curare was employed, but the crude drug was very uncertain in its action, and not a few fatalities occurred.

Richard Gill,[3] an American who owns a large ranch in Ecuador, obtained the confidence of his Indian neighbors to such a degree that by 1937 they allowed

From the Subdivisions of Anesthesia and Thoracic Surgery, Department of Surgery, University of California Medical School.

Read at the Twenty-sixth Annual Meeting of The American Association for Thoracic Surgery, Detroit, Mich., May 29, 30, and 31, 1946.

Research financed in part by the Christine Breon Research Fund.

him to observe the secret manufacture of their arrow poison. After investigation, it was found that the active ingredient was *Chondrodendron tomentosum.* He has been able to obtain a large and continuous supply of the crude drug from the Indians, which the Squibb Company purifies and markets under the trade name of Intocostrin.

In 1940, A. E. Bennett[4] reported the use of small doses of curare to "soften" the convulsions of metrazol shock therapy for psychoses and thus prevent the fractures which had proved a serious complication of this form of therapy. In 1942, Griffith and Johnson[5] of Montreal and Stuart Cullen of Iowa used similar small doses to produce muscular relaxation during cyclopropane anesthesia for abdominal surgery. Cullen[6] published a very enthusiastic report of his work in a series of 200 cases in 1943.

A tremendous volume of literature has been published during the last seven years on the subject of curare. This drug has been advocated and tried for numerous conditions, the most important of which are mentioned here, and, in addition, the diagnosis of myasthenia gravis, the production of relaxation for endoscopy of various types, and the treatment of acute poliomyelitis and spastic paralysis. The extensive use of curare has been limited, however, to the prevention of convulsions during shock therapy and the production of relaxation during cyclopropane anesthesia. In all this time there has been little experimental work on the physiologic effects of the drug. McIntyre and King of Nebraska[7] have published several articles on the pharmacology of curare and allied substances. Alexander Partos,[8] in 1930, reported the occurrence of glycosuria in curarized frogs, and Feitelberg and Pick of Vienna[9] in 1942 reported certain changes in the electroencephalograms of pithed, heavily curarized frogs, which somewhat resembled the changes occurring during narcosis. The pharmacologists of the Squibb Company have found by biologic methods that after the administration of curare, 40 to 60 per cent is excreted in the urine. This work has not been published. Curare has been found by Gross and Cullen[10] to cause loss of peristalsis and muscle tone in the stomach and small bowel, a fact of considerable importance in abdominal surgery. However, the vast bulk of the literature consists of ever-increasing series of cases reported by various anesthetists, the less eminent the anesthetist, the larger the series and the fewer the complications, culminating in an article published in March, 1945, by a nurse technician[11] reporting 751 cases with no complications whatsoever.

To our knowledge, this is the first report of the use of curare in anesthesia for thoracic surgery, with the exception of a preliminary report by one of us.[12]

In the winter of 1943, after reading an article by Cullen[6] in which he contended (as do most authors) that the danger of curare lay in its ability to cause complete respiratory paralysis, we conceived the idea of making use of this property of the drug to obtain the apnea necessary for so-called "controlled respiration" in thoracic surgery. This technique would allow the surgeon to employ the cautery inside the pleural cavity since no ignitable agent would be necessary. We do not believe curare to have anesthetic properties and accordingly our plan was to use nitrous oxide for anesthesia and curare for relaxation.

LIBRARY
BOSTON UNIVERSITY
SCHOOL OF MEDICINE

We considered the reported experimental work on curare inadequate; therefore, in March, 1944, we began administering it to unanesthetized dogs premedicated with atropine. Sufficient drug was given to produce apnea for two to eight hours. A series of fifty dogs was run and blood sugar determinations and electrocardiograms were taken on many of them. The blood sugar was found to rise rapidly to 200 to 300 per cent of the initial reading. The electrocardiographic tracings showed certain changes as to the significance of which the cardiologists have been unable to come to any definite conclusions. The mortality of this group was 12 per cent; 6 per cent of the dogs died of atelectasis or pneumonia after having returned to the cage. The others died accidental deaths: hypoxia, too much prostigmine, and failure to intubate.

A beginning has been made on the problem of electroencephalograms in dogs before and after heavy doses of curare, with the idea of proving whether or not this agent has a narcotic effect, but our series is yet too small to warrant any conclusions.

The technique of curare administration as previously described by us[12, 13] is as follows:

The patient is heavily medicated with a short-acting barbiturate, morphine, and scopolamine, on the morning of the operation. It is our desire that the patient reach the operating room only sufficiently awake to move from his bed to the operating table. The anesthesia is now begun. Nitrous oxide and oxygen are administered by means of a face mask. If any difficulty is encountered in producing anesthesia smoothly, sufficient Pentothal sodium is injected intravenously to attain satisfactory anesthesia. Particular notice is taken of the proportions of nitrous oxide and oxygen necessary to keep the patient satisfactorily anesthetized and well oxygenated during induction. When the patient's jaw relaxes, a pharyngeal airway is inserted and the anesthetist's ability to inflate the lungs is tested by pressure on the breathing bag. Our rule is never to administer curare to a patient unless we are certain that we can carry out efficient artificial respiration by means of a face mask and breathing bag. A quantity of curare* calculated to be sufficient to produce apnea is then administered intravenously to the patient. The usual adult requirement is 200 mg. Apnea develops in from thirty seconds to two minutes, following the injection of curare. The patient's lungs are then rhythmically inflated by gentle intermittent pressure on the breathing bag. After approximately five minutes, when the patient has reached a maximum state of relaxation, the mask is removed and an orotracheal tube with an inflatable cuff is inserted through the larynx into the trachea under direct vision. The profound muscular relaxation that follows the intravenous injection of curare usually makes intubation an easy maneuver. Sometimes on laryngoscopy the vocal cords will be seen to be in spasm, but the musculature of the larynx shares the general muscular weakness produced by curare and the cords can easily be separated by the soft rubber endotracheal catheter. If the dose of curare has been too small and the patient's jaw is insufficiently relaxed for easy intubation, "controlled respiration" by

*Intocostrin, manufactured by E. R. Squibb & Sons, New York, N. Y.

means of the airway, mask, and bag, with nitrous oxide and oxygen, is continued, while another 100 mg. of curare is given intravenously.

After the endotracheal tube is correctly inserted into the trachea it is connected to a canister of soda lime and a breathing bag, the delivery tube from the gas machine is attached, and anesthesia is continued, using the same concentration of nitrous oxide and oxygen that was previously determined would keep the patient well anesthetized and well oxygenated. This is an important point, since once the muscular paralysis of curare has set in, the signs of anesthesia, all of which are muscular, are completely masked. The patient is now placed in the desired position on the operating table and the operative site is prepared and draped in the usual manner. A continuous slow drip of 5 per cent glucose in water is started in an arm or hand vein. A three-way stopcock with a Luer syringe of curare on the side arm is connected in circuit with the slow drip and so placed that it will be conveniently within reach of the anesthetist. A cut-down is done on an ankle vein and a slow drip of normal saline is started to allow for the administration of blood or plasma. The operation is begun.

In children under 15 years of age, certain changes in the standard technique have proved advantageous. The child is medicated heavily with morphine and scopolamine but without any barbiturate. We feel that children are difficult to anesthetize with nitrous oxide and oxygen alone, without hypoxia. Therefore we administer a basal narcotic, tribromoethanol (avertin) in doses of 100 to 150 mg. per kilogram before the inhalation anesthesia is begun. Enough cyclopropane is then given by means of a face mask to produce second plane anesthesia, the endotracheal tube is inserted, and anesthesia is continued with a high flow of nitrous oxide and oxygen without rebreathing. A cut-down on an ankle vein is done, and a very slow continuous drip of 5 per cent glucose in water is started. Just before the pleural cavity is opened, enough curare is injected into the tubing of the intravenous drip apparatus to stop respirations. This will be 40 to 60 mg. in a child 2 to 4 years of age. A T-tube is then connected to the end

CHART 1.—AGE OF PATIENTS, DURATION OF ANESTHESIA, AND TOTAL DOSE OF CURARE

	AVERAGE	MAXIMUM	MINIMUM
Age in Years	40.7	72	1
Duration of Anesthesia	5 hr. 11 min.	10 hr. 40 min.	1 hr. 45 min.
Dose of Curare (in mg.)	310.5	790	40

of the endotracheal catheter and a continuous flow of nitrous oxide and oxygen is blown from the machine into the opposite end of the tube. The lungs are inflated by intermittently shutting off the side arm of the tube by the anesthetist's thumb and deflated by releasing this pressure, careful watch being kept by the anesthetist on the chest wall or lung to prevent overinflation. Apnea is maintained by repeated injections of curare into the intravenous drip tubing as long as the pleural cavity is open. The reason we do not give fluid in two veins, as in adults, is because of the possibility of giving a small child more fluid than he can handle during an operation of from four to six hours.

The adult patient will usually resume spontaneous respiration twenty to thirty minutes after the initial 200 mg. of curare. When the respirations are

sufficiently deep to provide adequate inflation of the lungs, the patient is allowed to breathe spontaneously until the surgeon is ready to enter the pleural cavity. An additional dose of curare sufficient to stop respiration is then administered. It will usually be found that 40 to 60 mg. of curare will produce apnea at this time. When respiratory depression appears, intermittent manual pressure of the breathing bag is resumed, since excess carbon dioxide or lack of oxygen may

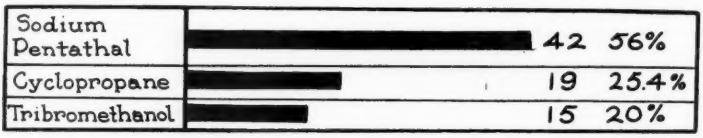

Chart 2.—Patients receiving supplemental anesthetic agents in addition to nitrous oxide and oxygen and curare.

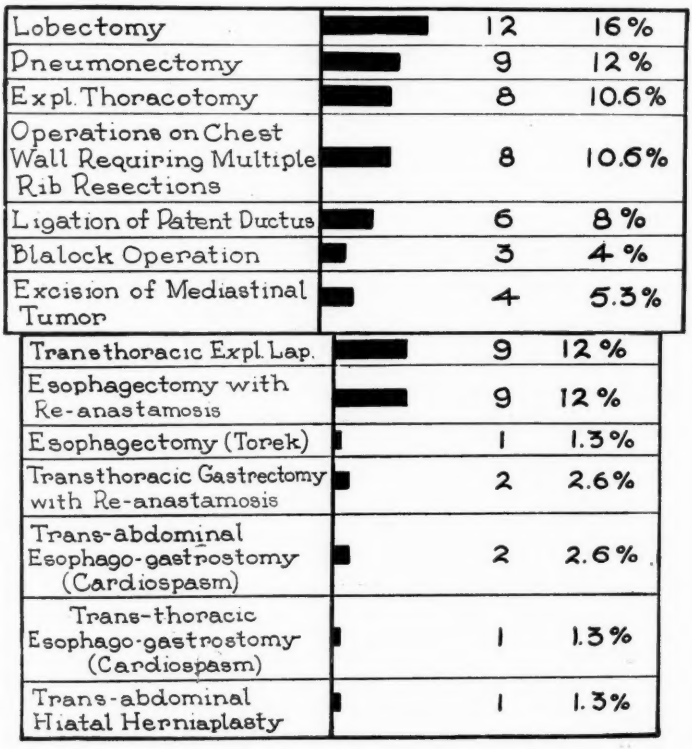

Chart 3.—Operative procedures: types of cases (lung, heart, and miscellaneous, above, and gastrointestinal, below).

cause the patient to attempt spontaneous respiration even though the dose of curare is adequate to produce apnea. If the patient continues to breathe spontaneously five minutes after the first dose, a second dose is administered; additional quantities are given at five-minute intervals until apnea is attained.

Whenever respiration is resumed by the patient, 20 to 40 mg. of curare (or more if necessary) are given, thus maintaining the desired respiratory arrest as long as the pleural cavity is open.

If the sedative effect of the preoperative medication wears off, as frequently occurs during long operations, it will now be found that the anesthetic mixture is no longer sufficient to keep the patient anesthetized. This lack of anesthesia will not be evidenced by the usual signs of light anesthesia, since, as was previously explained, the signs are masked. Diaphragmatic contractions, slight muscular twitching, movement of the facial muscles, or a rise in blood pressure are signs of too light a plane of anesthesia in a completely curarized patient. These phenomena are indications for an additional dose of morphine, preferably administered intramuscularly.

The patient is kept in apnea by means of these small, repeated doses of curare throughout the time the pleural cavity remains open. When the surgeon has effected an airtight closure of the pleural cavity, pressure on the breathing bag is discontinued and the patient is allowed to build up carbon dioxide in his blood stream. Spontaneous respiration will be resumed usually in about a minute. If spontaneous respiration is not resumed by the time slight cyanosis occurs, controlled respiration is again instituted. This routine is repeated every few minutes until the patient breathes spontaneously. The patient is now allowed to breathe for himself, but until the intercostal muscles are functioning adequately, an occasional squeeze of the breathing bag will prevent the upper lobes from becoming atelectatic.

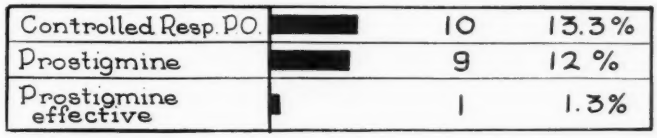

Chart 4.—Patients requiring resuscitation at completion of operation.*

When the anesthetist is satisfied that intercostal activity has sufficiently returned, and it is desired to terminate the anesthetic, the breathing bag is emptied of its nitrous oxide-oxygen mixture and filled with air, and the lungs are then manually inflated several times with air, after which the breathing bag is disconnected from the endotracheal tube. Secretions are thoroughly aspirated from the patient's tracheobronchial tree by means of a suction catheter inserted through the endotracheal tube. It is at this time that the patient usually awakens. Secretions are similarly aspirated from the oropharynx, and, when clean, the endotracheal tube is removed.

Occasionally a patient is encountered whose intercostal muscles have not recovered their power of contraction by the time the operation is ended (Chart 4). This condition results either because of overmedication with a barbiturate, or because it was necessary to give the patient large doses of curare in order to keep him in apnea throughout the time the pleura was open. In these

*Prostigmine was used in nine cases, but was effective in only one.

cases the anesthesia is stopped and the patient's lungs are inflated rhythmically with oxygen, or a mixture of air and oxygen, delivered through the endotracheal tube. The endotracheal tube should under no circumstances be removed or the patient returned to the ward until the anesthetist is satisfied that the patient's intercostal muscles are contracting vigorously. If this rule is disregarded the patient will almost invariably develop atelectasis. Prostigmine has proved to be ineffective in our hands in hastening the return of intercostal muscle contraction (Chart 4).

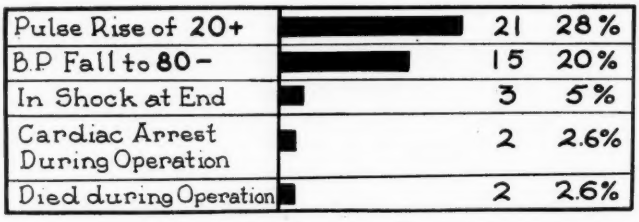

Chart 5.—Complications during surgery.*

The patients are usually awake and able to answer questions before leaving the operating table, even after operations six hours or more in duration. However, it must be remembered that the residual muscular weakness persists for several hours and makes careful aftertreatment necessary. The patient should be placed in bed on his operated side and turned frequently from one side to the other. Coughing should be encouraged. Oropharyngeal oxygen should be given if indicated by the presence of dyspnea, rapid pulse, or cyanosis.

Seventy-five cases in which this type of anesthesia was employed are summarized in the accompanying tables.

SUMMARY

This communication details our technique of administering curare with nitrous oxide and oxygen for the purpose of providing anesthesia in major thoracic operations. The fact that these agents are nonexplosive offers a decided advantage to the surgeon in making possible the use of the high frequency current throughout the entire surgical procedure. The additional attractive features of this type of anesthesia are that the patients remain in excellent condition throughout operations that require many hours, and that they are awake and responding consciously by the time they reach the ward. The average date of ambulation and date of discharge from the hospital (as shown in Chart 6) in our opinion bears out our contention that the patient's physiology is upset very little by the use of nitrous oxide in combination with curare. The general magnitude of the operative procedure is mirrored in the duration of anesthesia which averages five hours eleven minutes (Chart 1).

Seventy-five cases, representing chiefly major intrathoracic operations, have received this type of anesthesia and a study of these cases has been presented. There have been eight hospital deaths in this group of seventy-five.

*See Chart 9 for causes of death.

It is our opinion that the anesthetic agents may have had a direct bearing in two of these deaths (Cases 6 and 7, Chart 9). Both of these patients had difficulty coughing up their bronchial secretions following operation and it is possible there may have been residual weakness of the respiratory muscles following curare. We are not able to prove or disprove this suspicion but believe it should

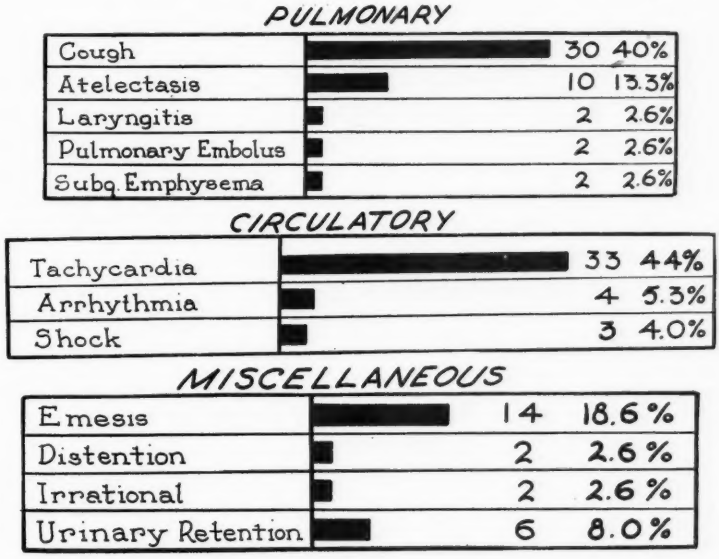

Chart 6.—Postoperative complications.*

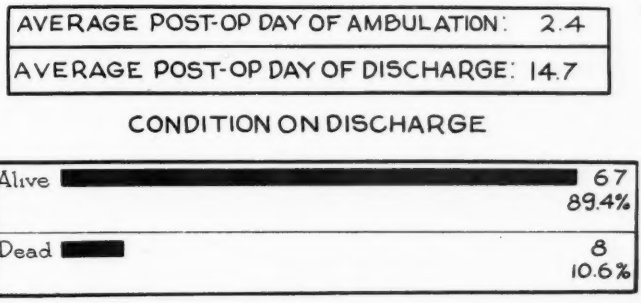

Chart 7.—Ambulation and discharge.†

be noted as a possible sequence or complication of high curare dosage. The two patients just enumerated had had several ribs removed and there was some paradoxical swing in spite of the firm, supportive, adhesive dressing. Death occurred on the fourth and tenth postoperative days in spite of vigorous at-

*If the pulse rate went above 120, the patient was classified as having tachycardia.
†Day of discharge refers to discharge from hospital.

tempts to keep the respiratory passages clear of secretions. Necropsy examination in both instances failed to demonstrate accurately the cause of death.

Our observations on dogs that had received large doses of curare point to a rapid disappearance of the paralyzing action of this drug and it is our opinion that curare has no late accumulative effect. It is quite possible that curare had no direct bearing on the cause of death in Cases 6 and 7.

The significant complications during the actual operations are reported in Chart 5. The cause of death of the two patients that expired on the operating table is given in Chart 9 (Cases 1 and 2). The two instances of temporary cardiac arrest warrant comment. This complication occurred the first time during the operation of pneumonectomy in a 65-year-old man. The cardiac arrest was momentary and the normal heart rhythm was almost immediately re-established by cardiac massage. Cardiac arrest also occurred in the case of a 4-year-old baby girl undergoing the Blalock operation. The heart stopped at

CHART 8.—LIVER AND KIDNEY FUNCTION

	AVERAGE, PREOPERATIVE	AVERAGE, POSTOPERATIVE
Intravenous Hippuric Acid (50 cases)	1.04	0.89
Phenolsulfonphthalein (44 cases)	75.6%	75.9%

Electrocardiograms. No significant change between N_2O-O_2 anesthesia ± pentothal and N_2O-O_2 anesthesia ± pentothal + 200 mg. curare (35 cases).

CHART 9.—CAUSE OF DEATH

CASE	AGE	DIAGNOSIS	OPERATION	TIME OF DEATH	CAUSE	AUTOPSY FINDING
1	20	Bilateral bronchiectasis	Lobectomy right middle lobe and right lower lobe	During operation	Hypoxia from excessive secretion	No autopsy
2	16 mos.	Mediastinal tumor	Excision of mediastinal tumor	During operation	Hemorrhage + possible lung injury	Negative
3	55	Bronchogenic carcinoma, left lower lobe	Pneumonectomy, left	20 min. P.O.	Hemorrhage from pulmonary artery	Antemortem clot in superior vena cava and heart
4	4	Tetralogy of Fallot	Blalock operation	8 hrs. P.O.	Pulmonary edema	Pulmonary edema
5	40	Bronchogenic carcinoma, left lung	Pneumonectomy, left	3 days P.O.	Cerebral metastases	Cerebral metastases
6	38	Tbc. with cavitation	2nd stage thoracoplasty with apical mobilization	4 days P.O.	Inability to cough out secretions	Negative
7	60	Bronchogenic, carcinoma, left lung	Pneumonectomy, left	10 days P.O.	Inability to cough out secretions	Pulmonary edema
8	51	Carcinoma of stomach	Transthoracic gastrectomy Resection of distal one-third of esophagus Splenectomy Esophagojejunostomy Jejunojejunostomy	13 days P.O.	Pulmonary embolis	Pulmonary embolus

three different periods during this operation but rhythm was re-established by cardiac massage. This latter patient is shown as Case 4 in Chart 9, and as shown in the table the patient expired eight hours following surgery.

Auricular fibrillation occurred in three patients during the postoperative period and auricular flutter with 2-to-1 block in one other patient. These arrhythmias were all of a temporary nature and did not prolong the periods of hospitalization following operation. Pulmonary complications following operation were not severe and the average day of discharge in those cases suffering from atelectasis was 14.4 days. (Charts 6 and 7.) It is quite possible that all of the patients in this entire series received a certain amount of protection from the chemotherapeutic agents (penicillin and sulfadiazine) that were used almost routinely before and after operation.

Liver and kidney function studies have been outlined (Chart 8). Insofar as we could determine, the anesthetic agents under discussion produced no significant changes in the two function tests used. Electrocardiograms were taken on thirty-five patients before and after they received 200 mg. of curare intravenously. Here again no significant changes were noted.

CONCLUSION

Nitrous oxide anesthesia combined with curare for the production of apnea have been satisfactory anesthetic agents in our experience for use in major thoracic surgical operations. The enumerated results in seventy-five cases are sufficiently encouraging, we believe, to warrant our continued use of these agents. It is our hope that this report will lead to a more general use of nitrous oxide with curare for anesthesia in thoracic surgery.

REFERENCES

1. Raleigh, Sir Walter: The Discovery of Guiana, London, 1596.
2. Bernard, Claude: Bull. gén. de thérap. med. et chirurg., 1865. Lefons sur les Substances Toxiques, Paris, 1857.
3. Gill, Richard: White Water and Black Magic, New York, 1941, Henry Holt & Company.
4. Bennett, A. E.: J. A. M. A. **114**: 322, 1940.
5. Griffith, H. R., and Johnson, G. E.: Anesthesiology **3**: 418, 1942.
6. Cullen, Stuart: Surgery **14**: 261, 1943.
7. Mc Intyre, A. R., and King, R. E.: Science **97**: 69, 1945.
8. Partos, Alexander: Pfluger's Arch. f. d. ges. Physiol. **223**: 40, 1930.
9. Feitelberg, Sergei, and Pick, Ernest: Proc. Soc. Exper. Biol. & Med. **49**: 654, 1942.
10. Gross, A. E., and Cullen, S. C.: Anesthesiology **6**: 231, 1945.
11. Borromea, Sister M.: Ann. Meeting of A. A. of Nurse Anesthetists, 1945, Chicago.
12. Harroun, P., and Hathaway, H. R.: The Use of Curare in Anesthesia for Thoracic Surgery: Preliminary Report, Surg., Gynec. & Obst. **82**: 229, 1946.
13. Harroun, P., Beckert, F. E., and Hathaway, H. R.: Anesthesiology **7**: 24, 1946.

DISCUSSION

DR. JOSEPH A. WEINBERG, Van Nuys, Calif.—Dr. Stephens, Dr. Harroun, and Dr. Beckert are to be congratulated on giving us a new method of anesthesia for thoracic surgery which overcomes difficulties which are inherent in other types of anesthesia. I have used the method several times since witnessing its use by the essayists, and have been impressed by its value in allowing electrocoagulation, and in otherwise making thoracic surgery easier.

However, I believe that its proper place in anesthesia cannot be evaluated for some time. As with any new method, we must wait a considerable length of time and see a great number of cases before the method can be properly evaluated. Every effort should be made to minimize the dosage by reserving it for the time that it is actually needed. Satisfactory anesthesia may be had at the beginning and at other phases of the operation by intravenous pentothal sodium as an adjunct to the nitrous oxide anesthesia. One may thus withhold the use of the curare for such times as apnea is needed for the more delicate maneuvers.

This is very important, because we are not certain that tissues can be maintained in the proper state of oxygenation during states of apnea.

I would like to know whether or not the term atelectasis as used by the essayists refers to massive atelectasis. If it does, this is one of the meanest complications that we may have to combat and successfully overcome if this is to be a useful method for general thoracic surgery procedures.

DR. ALFRED GOLDMAN, Los Angeles, Calif.—I have operated on two of the patients in this series. One of them presented a problem which I think would be very difficult without curare, or at least would bring up difficulties that did not arise during this operation, since whenever it is necessary to open the mainstem bronchus and keep it open for a period as long as sixty seconds, the anesthetist has difficulty in maintaining gas in the bag because it leaks out so rapidly through the open bronchus.

(Slide.) This woman was 38 years of age with bronchial adenoma residual in the left stem bronchus four years after supposed complete bronchoscopic removal. The artist's drawing shows the residual tumor. He has drawn it lower than it actually extended.

At operation the lobe was completely mobilized; adhesions were very dense and numerous, and the procedure was prolonged. It would have endangered her life to have continued to attempt to remove the upper lobe, which was densely adherent. Therefore, it was decided to open the bronchus, remove the tumor by a U-shaped incision of the stem bronchus and the lower lobe bronchus, just at the site of the upper lobe opening, completely encircling the endomural adenoma.

During the time that the bronchus was opened this patient did not have any mediastinal flutter which we would have expected if the curare had not only paralyzed her homologous left but also her right diaphragm.

(Slide.) This shows the tumor that was removed. This is the actual specimen taken cross-section. The tumor is 2.0×1.0 cm.

(Slide.) This shows the lobectomy specimen that was removed at the same time. This point is the incision that was made across the bronchus where the right-angle incision lay the bronchus completely open. Note the cystic bronchiectasis.

In conclusion, I would like to say that I think that curare has a definite advantage wherever it is necessary to open the bronchus and keep it open for any length of time during operation in the open chest.

DR. RALPH A. DORNER, Iowa City, Iowa.—I have the great advantage of working with Dr. Stuart Cullen, whom the essayist has mentioned. Dr. Cullen has done a great deal of work with curare at the University of Iowa, and we, since my return from military service, have used curare in a fairly large series of thoracic cases.

I feel that with the use of curare in thoracic work, there are many benefits to be derived, as have been listed, and it is my observation that our patients receiving curare have not suffered from any particular complications due to curare per se. I feel that our postoperative complications have not been greater than with cyclopropane, ether, or ethylene anesthesia.

We make it a point to bronchoscope routinely every major postoperative thoracic case except thoracoplasties. Any patient who has had a pulmonary resection is bronchoscoped immediately postoperatively, and it is our feeling that since instituting this practice many of the postoperative complications, pulmonary in nature, such as atelectasis, have been avoided.

We have no reason to feel that curare is particularly dangerous to the patients or that it causes unusual complications.

DR. H. BRODIE STEPHENS, San Francisco, Calif.—The technique of administering curare as outlined by Dr. Harroun is, so far as I know, original.

This type of anesthesia has proved to be the most satisfactory to date for major intrathoracic procedures in our hands. We are inclined to believe that curare will become generally accepted as a valuable supplement to anesthesia in thoracic surgery.

DR. PHYLLIS HARROUN, San Francisco, Calif.—Dr. Weinberg is quite right about minimizing the doses of curare that are used. We did not attempt to do that. We have no fear of it whatsoever, and we were anxious to see what happened with tremendous doses.

It is quite possible that some other method of intubation would be better than giving the patient so many milligrams of curare that he cannot react, and then inserting the tube. We did that to see what would happen, and to get our electrocardiographic tracings without any other variable factors.

This technique was worked out for thoracic surgeons, and we hope that it will be found to be advantageous. Our greatest hope is that it will be of use in the future.

SURGICAL TREATMENT OF MYASTHENIA GRAVIS

O. Theron Clagett, M.D.,* and L. M. Eaton, M.D.,†
Rochester, Minn.

SINCE 1901, when Weigert[13] reported finding a thymic tumor in a patient who had died of myasthenia gravis, extensive efforts have been made to establish a definite relationship between the thymus gland and myasthenia gravis. It has been a difficult problem, because actually we know so little about either the organ or the disease. An editorial[6] in the *Lancet* has expressed very well the problem involved in the attempt to associate the gland with the disease. "The thymus gland has remained an enigma. Endocrinologists have wooed it in vain. Physiologists and pathologists have drawn away from it baffled. Not even the anatomists and histologists have spoken of it with their customary precision. A mystery of another kind is hidden under the name myasthenia gravis, a disease which is uncommon but none the less notorious for its resistance to both rational explanation and treatment."

GENERAL CONSIDERATIONS

Despite the difficulties involved in establishment of a relationship between the thymus gland and myasthenia gravis, strong evidence of such an association has come from pathologists. Bell[1] Miller,[8] and Norris[9] have found thymic abnormalities in such a high percentage of patients dying of myasthenia gravis, that is, approximately 50 per cent, that it seems justifiable to conclude that some association does exist.

The first surgical attempts to cure patients of myasthenia gravis by removal of the thymus gland were made by Sauerbruch.[11] These attempts were carried out before neostigmine (prostigmine) had been developed for the medical treatment of the disease and before the technique of thoracic surgery had advanced to its present status, and were complete failures. However, in 1939, Blalock and his associates[4] reported success in the treatment of myasthenia gravis by removal of a tumor from the anterior portion of the mediastinum; this tumor, although not histologically verified, was almost certainly of thymic origin, and interest in the subject revived. Considerable literature[2, 10] on various phases of the subject has accumulated since that time.

When one is dealing with a disease such as myasthenia gravis, in which the course is unpredictable and in which spontaneous remissions are prone to occur, it is dangerous to attempt to draw conclusions based on only a few cases. However, at the Mayo Clinic, since our intensive interest in the relationship of myasthenia gravis to the thymus gland began in 1941, we have performed operations on the thymus gland and carried out careful follow-up study of the subsequent course of the disease in a sufficiently large number of cases to warrant a report of our experience to date. In our early experience we advised operation

Read at the Twenty-sixth Annual Meeting of The American Association for Thoracic Surgery, Detroit, Mich., May 29, 30, and 31, 1946.

*Division of Surgery, Mayo Clinic.
†Department of Neurology and Psychiatry, Mayo Clinic.

only in those cases in which a thymic tumor was demonstrable roentgenologically. Later, we also began to perform thymectomy in cases in which there was no evidence of tumor.

THE PRESENT SERIES

This report is based on a series of thirty-two patients with myasthenia gravis who have been followed for six or more months since operation upon the thymus gland. The entire series consisted of 191 patients, 159 of whom were not operated on. In fifteen of the thirty-two cases thymic tumors were found at operation. In seventeen cases no tumor was found. In all but one of these a good-sized thymus gland was found and removed. Since there is insufficient time in which to report and discuss each case at this writing, the results are presented in tabular form (Tables I and II). More complete data will be presented in a forthcoming paper (by McDonald, Good, and ourselves). We shall confine ourselves at this time to the surgical aspects of the problem and the results of our experience to date at the clinic.

TABLE I. RESULTS OF OPERATION FOR REMOVAL OF THYMIC TUMOR OR OF THYMUS GLAND ON THIRTY-TWO PATIENTS WHO HAD MYASTHENIA GRAVIS

REMOVAL OF TUMOR (THYMOMA)	NO.	TOTALS
Patients	15	15
Postoperative deaths	1*	
Little if any improvement	3	
Moderate improvement	4	
Considerable improvement	4	
Essentially well or in complete remission	3	
REMOVAL OF THYMUS GLAND (NO TUMOR)		
Patients	17	17
Postoperative deaths	3†	
Little if any improvement	6	
Moderate improvement	6	
Considerable improvement	2	
Total for series		32

*Patient died three days after operation.
†Patients died three days, three months, and six months, respectively, after operation.

TABLE II. COMPARATIVE RESULTS IN THREE REPORTED SERIES OF REPORTED CASES OF MYASTHENIA GRAVIS

SERIES	CASES	TUMORS	DEATHS		COMPLETE REMISSION	IMPROVEMENT			TOTAL WELL, IMPROVED, OR NOT IMPROVED
			OPERATIVE	POSTOPERATIVE		CONSIDERABLE	MODERATE	LITTLE OR NONE	
Keynes[7]	51	6	8	5	9	11	8	5	33*
Blalock[3]	20	2	3	1	3	5	5	3	16
Clagett and Eaton	32	15	2	2	3	6	10	9	28

*Keynes had fifty-one patients, of whom thirteen died operatively or postoperatively, leaving thirty-eight living persons. Keynes excluded certain of these thirty-eight patients, for reasons set forth in his paper, so that the total number of patients well, improved, or not improved became thirty-three.

We have been fortunate in having a rather large series of thymic tumors. Eleven of our patients with tumors were males and four were females; of those who did not have tumors, twelve were females and five were males. The ages

of the patients who had tumors averaged 42.3 years, ranging from 26 to 57 years; only four were less than 40 years old. On the other hand, the ages of patients who did not have tumors averaged 31.4 years, ranging from 16 to 67 years; thirteen of the seventeen patients in this group were 30 years old or less. Approximately half of the myasthenic patients coming to the Mayo Clinic are less than 40 years old, and in this group females predominate more than two to one; in the group of patients more than 40 years of age the ratio is reversed. Consequently, the distribution according to sex of these patients, when compared with that of other myasthenic patients of the same age, does not differ essentially from the distribution according to sex of the total group of myasthenic patients. We conclude, therefore, that tumors are found more frequently in the older age group of myasthenic patients than in the younger group, and consequently, that the proportion of males is higher than that of females in this group.

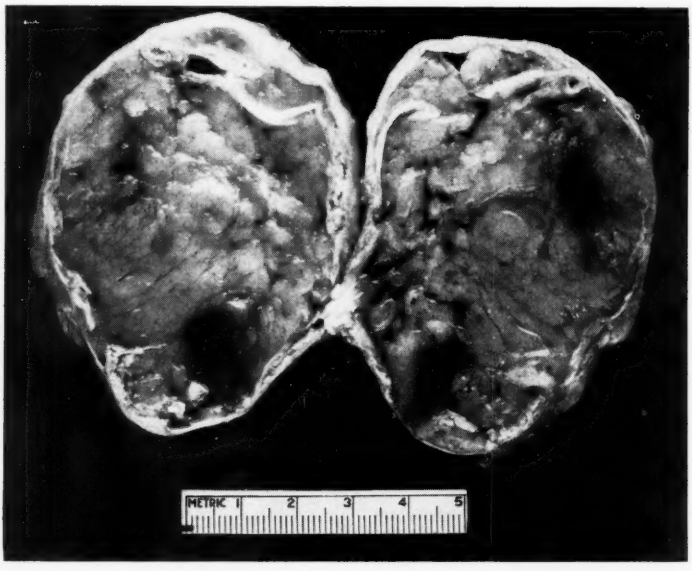

Fig. 1.—Open cut surface of large thymic tumor.

In eight cases thymic tumors were removed without any attempt to remove the entire thymus gland. In two cases the entire thymus gland as well as the thymic tumor was removed. In five cases the tumor of the thymus gland had invaded surrounding structures such as the pleura, lungs, and even large blood vessels, making complete removal of the gland impossible. In these instances as much of the tumor as possible was removed, or else large specimens were taken for pathologic examination.

In the group of patients who did not have thymic tumors, a good-sized thymus gland was found in every case but one. In retrospect, we believe the thymus

gland may have been overlooked in this one case. The patient was one of the earlier ones in our experience, and we had not learned that the thymus may lie behind the left innominate vein instead of in front of it. We have had two patients since whose thymus gland was found definitely to lie behind the vein, and Keynes has reported a similar experience. The duration of hospitalization of these patients was seven to twenty days, with an average hospitalization of only ten days. There was one postoperative death; the patient was 67 years old and probably would not have been operated upon if roentgenologic examination had not indicated a small thymic tumor. No tumor was found (this represents the only error in diagnosis made on roentgenologic examination in our series). Two patients survived operation without difficulty, but died a few months later of myasthenia gravis.

Fig. 2.—Cystic and solid thymus gland, with cross section of thymic tumor.

In assessing the effects of thymectomy on these patients who had myasthenia gravis, we have divided the patients into two main groups; (1) those subjected to operation for removal of the thymic tumor (thymoma), and (2) those subjected to operation for removal of the thymic gland (no tumor). We have divided each of the two main groups into the following subgroups: (a) those who have died since operation, (b) those who are little, if any, improved, (c) those who are moderately improved (in this group are included those who continue to have symptoms of myasthenia gravis but who have been able to reduce substantially the amount of neostigmine required for maintenance of a comparable degree of activity, or have been able to increase substantially the amount of work they can accomplish while taking essentially the same amount of medication), (d) those who are considerably improved (in this group the patients

continue to have definite symptoms of myasthenia gravis, but have been able to increase the amount of activity they were able to engage in to a considerable degree, while taking much less neostigmine than they formerly required), and (e) those who are essentially well, or whose disease is in complete remission.

It is interesting to compare our experience with that reported recently by Keynes[7] and by Blalock.[3] Keynes has reported a series of fifty-one cases and Blalock a series of twenty cases in which operation on the thymus gland was performed, compared to our thirty-two cases (Table II). They have not specified the duration of their follow-up study after operation, but it seems likely that the thirty-three patients of Keynes and the sixteen of Blalock used for evaluation of the effect of operation are comparable to the twenty-eight patients in our series who have survived sufficiently long for evaluation of results. In Table II is indicated the difference in our experience. The difference in incidence of tumors is understandable because in our early experience we limited operation to those patients who had thymic tumors. We believe the difference in operative fatality can be attributed to our choice of patients for operation and our attention to detail in the preoperative and postoperative management of these patients. We are unable to account for the differences in the results of operation in the series. Keynes' results are considerably better than ours in this regard. Keynes has voiced the opinion that the prognosis is very poor for those patients who have tumor. Only two of his patients who had tumors were alive at the time he wrote, and he also believed that patients who have tumors do not respond so well to neostigmine as do other myasthenic patients. In our experience the patients who have tumors have done better than patients with hyperplasia, so far as their myasthenia is concerned.

Although we have not set up a specific control series at this time for comparison, we gain the distinct impression that the thirty-two patients who underwent surgical treatment have fared much better than the remaining 159 of our series who were not treated surgically.

Of the fifteen patients who underwent operation and who had thymic tumors, eleven have shown unequivocal improvement; seven to a marked degree (Table I). Of the seventeen who underwent operation for removal of the thymus gland, eight are definitely improved at the time of writing. Among the six in the latter group who show little if any improvement are four who have been followed only seven and one-half months or less. Experience with other patients treated surgically tells us that many of those who have shown considerable improvement made little progress in the first six to nine months after operation. Consequently, a longer period of observation may reveal that the results of thymectomy are better than they appear at the present time.

Two patients died during the immediate postoperative course. In two others, the progressive course of the myasthenia gravis was not changed, and they died three and six months after operation, respectively. We find no evidence that the condition of any patient who has survived the operation has been made worse by the procedure.

OPERATIVE PREPARATION

The preparation of the myasthenic patient is extremely important, since individuals with this disease are not good subjects for any surgical procedure. Because of difficulty in chewing and swallowing, many of these patients are thin, weak, and undernourished. Every effort should be made to improve the patient's nutritional status before operation. Usually, however, adequate doses of neostigmine will permit a patient to ingest a satisfactory diet. Occasionally, it may be necessary to resort to tube feeding. Because of their difficulty in swallowing, these patients sometimes aspirate food or oral secretions into their air passages. The best protection against this is adequate neostigmine therapy. Every precaution should be taken to protect these patients against respiratory infections. They are very susceptible to such infections, and often severe exacerbations of myasthenia result from respiratory infections. The amount of neostigmine administered to any myasthenic patient is determined by the severity of the disease. In this regard myasthenia is very similar to diabetes. The myasthenic patient soon learns to judge his neostigmine requirement just as the diabetic patient estimates his insulin needs. Without neostigmine to aid in controlling the severe manifestations of the disease, it would be impossible to perform operations on most patients who have myasthenia gravis.

We have profited by the suggestion that Blalock has made regarding the management of these patients. A period of a few days in the hospital before operation is essential. During that time, the neostigmine needs of the patient are carefully evaluated. Penicillin is given in order to minimize the danger of any respiratory infection, during or after the operation. We believe that this period of complete rest in the hospital is very beneficial.

All patients are fully informed before operation as to what they may expect in the postoperative course. They are told that they will be in an oxygen tent for twenty-four to forty-eight hours after operation, and that it may be necessary to place them in a Drinker type respirator for a time in their postoperative course. We agree with Blalock that in a case of severe myasthenia gravis in which operation is to be performed it is wise to put the patient in a respirator for a time preoperatively, so that he or she will become accustomed to it. All patients are warned not to expect miraculous relief of their disease, and are told that it will be necessary to continue to take neostigmine for an indefinite period postoperatively. A full discussion of all aspects of their disease and its management before operation does much to allay apprehension postoperatively. We avoid heavy sedation before operation. Just before going to surgery the patient receives 1.0 to 1.5 mg. of neostigmine, 1/8 grain (0.008 Gm.) of morphine sulfate, and 1/150 grain (0.00043 Gm.) of atropine.

OPERATION

We have used both cyclopropane and ether anesthesia for these procedures. We prefer a nitrous oxide-oxygen-ether combination at present. An intratracheal tube is used routinely. This permits aspiration of secretions from the tracheobronchial tree at any time during the operation, and prevents the occurrence of any difficulty should the pleura be opened during the operation. Most

operations can be accomplished entirely extrapleurally, but in some cases opening of the pleura is unavoidable. Neostigmine is available at all times and is administered hypodermically if any sign of respiratory difficulty develops during the operation. There is little loss of blood or occurrence of shock in most of these operations. All of our patients have tolerated their operative procedure without difficulty.

Fig. 3.—Hyperplastic thymus gland and thymic tumor.

We have used a variety of surgical approaches for our operations in these cases. In our early experience three tumors were removed through an anterior approach in which two cartilages were resected and in which the anterior part of the mediastinum was entered extrapleurally. This proved to be satisfactory as far as removal of the tumor was concerned, but of course did not permit exposure of the remainder of the thymus gland. This approach has been abandoned. For tumors too large to be removed through a sternum-splitting approach, we have used a posterolateral, transpleural approach, with resection of the fifth or sixth rib. This approach does not provide as good exposure of the entire thymus gland as the sternum-splitting incision that we prefer in most instances. In the latter approach, a vertical incision is made from the suprasternal notch to the xiphoid process. The fascia and soft tissues are dissected away from the surfaces of the manubrium, the Lebsche sternal chisel is inserted, and the sternum is split rather easily. We prefer to split the sternum for its entire length rather than to cut out into the fourth interspace, as some have

suggested. A self-retaining retractor is inserted and the segments of the sternum are spread apart, so that the anterior part of the mediastinum is exposed. Slight oozing from the sternal marrow occurs, but this has not been troublesome. At first glance, the thymus gland may not be visible. A slight amount of dissection through the mediastinal fat will disclose the gland. It is a pinkish-yellow, rather granular appearing organ. It has a thin and fragile but definite capsule. The gland usually is bilobate and joined in the center with two long, slender lobes extending up into the neck and broader lobes extending down along the sides of the mediastinum and over the upper pericardium. The lobes are often adherent to the pleura, so that the pleura may be opened inadvertently.

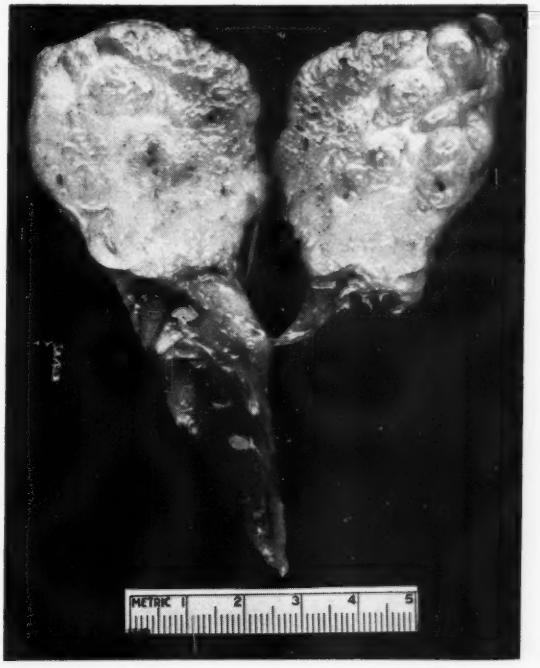

Fig. 4.—Cystic and solid, partially calcified thymic tumor.

The gland usually lies anterior to the left innominate vein where this vein crosses over to join the superior vena cava, but in two cases in our experience the gland lay behind this vein. There are a few small veins and arteries which must be ligated carefully. They apparently are branches of the internal mammary and inferior thyroid vessels. The largest vessels are two or more veins which enter the left innominate vein. The wound is closed by bringing the sternum together with encircling steel wire sutures and closing the superficial tissues in layers. Examples of thymic tumors and of excised thymus glands are seen in Figs. 1 through 7.

POSTOPERATIVE COURSE

The postoperative period is a critical time and requires the strictest vigilance. The margin of safety for these patients is not great. They are placed in an oxygen tent for as long as necessary, usually twenty-four to forty-eight hours. Penicillin is administered for several days postoperatively. Neostigmine is given hypodermically for the first twenty-four hours, in sufficient quantity to control the manifestations of the myasthenia. Often larger doses are necessary for a short time postoperatively than were necessary before operation. Neostigmine can be administered orally instead of hypodermically after twenty-four hours have passed, if the patient can swallow satisfactorily. An aspirator should be available to remove any accumulation of secretions in the nasopharynx and to prevent the aspiration of them in the tracheobronchial tree. Any evidence of

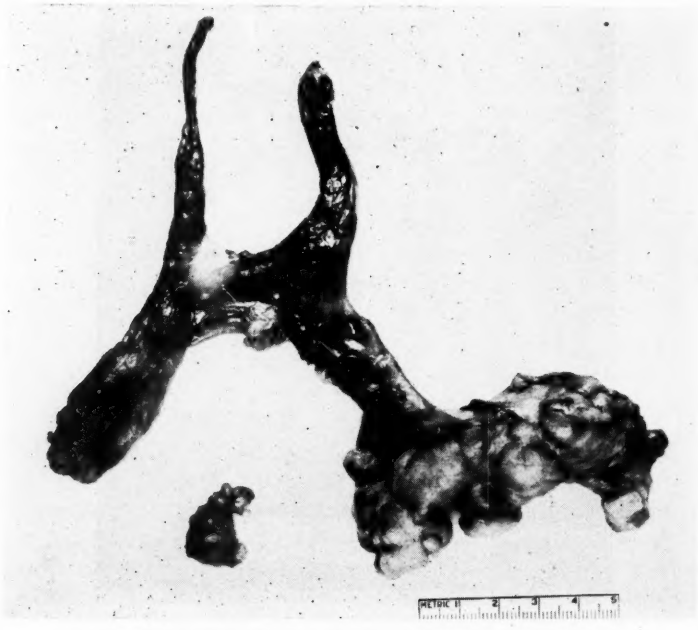

Fig. 5.—Hyperplastic thymus gland with tumor in left lower lobe.

anxiety, dyspnea, or respiratory embarrassment should be looked on with the greatest concern, since it is a sign of impending danger. A Drinker type respirator should be readily available whenever a myasthenic patient is operated on, and any patient who shows evidence of exhaustion or respiratory difficulty should be placed in the respirator immediately, even though his or her general condition appears to be good. Two patients undoubtedly were saved by use of the respirator. It is gratifying to observe the improvement that occurs when these patients are placed in the respirator. Their apprehension is relieved, they

relax, and rest, and begin to improve at once. While a patient is in the respirator it is safe to administer larger doses of sedative agents, if necessary, than it would be wise to give a myasthenic person under ordinary circumstances. Equipment should be readily available for aspiration of the tracheobronchial tree or for bronchoscopy, if there is evidence that secretion is accumulating in the air passages which the patient is not able to raise. In two of our cases it was necessary to perform bronchoscopy while the patient was in the respirator. If patients are not able to swallow satisfactorily in the postoperative period, a tube should be inserted through the nose into the stomach for administration of adequate fluids and nourishment. In most of our patients the postoperative course has not been difficult, but it is wise to be prepared for any eventuality. The course of these patients is unpredictable. Many of our patients have been up and about in three or four days. They are usually out of the hospital in ten to fourteen days.

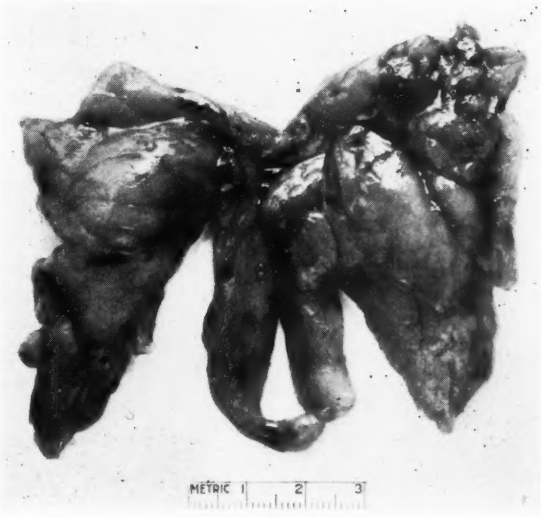

Fig. 6.—Large, hyperplastic thymus gland.

COMMENT

Our experience leads us to believe that the risk of operation in these cases is not great, provided all possible precautions are taken. Adequate therapy with neostigmine, penicillin to prevent infection, oxygen therapy, and the Drinker type respirator to prevent respiratory complications, aspiration or bronchoscopy to keep the tracheobronchial passages open and free of secretion, and the administration of fluids and nourishment by tube when necessary, can be used to obviate most of the difficulties and dangers inherent in operation on the myasthenic patient.

There are several interesting points in regard to the problems concerning myasthenia gravis and the thymus gland that deserve brief discussion.

One of the first problems confronting us was raised by the discrepancy between the frequency with which tumors of the thymus gland in myasthenic patients had been found at necropsy and the infrequency with which they had been found clinically. For the great majority of patients who had myasthenia gravis seen at the Mayo Clinic throughout the years, stereoscopic roentgenograms of the thorax had been made with the patient in the ordinary postero-anterior position. In spite of the large number of myasthenic patients who had undergone this examination, we were not able to find in previous records a single instance in which the diagnosis of thymic tumor had been made unequivocally. Apparently, the inability of the roentgenologists to diagnose tumors of the thymus gland in myasthenia gravis was not peculiar to this clinic.

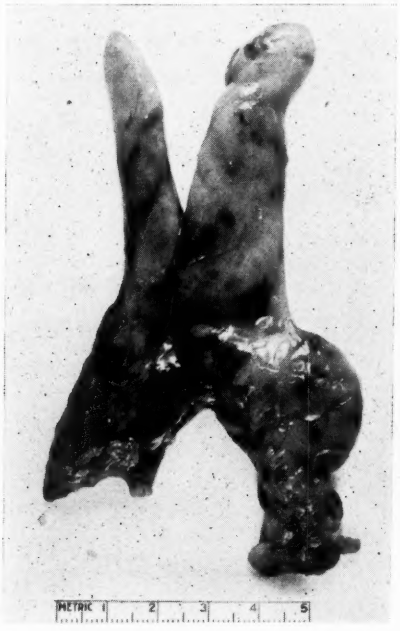

Fig. 7.—Large, hyperplastic thymus gland.

Viets and Schwab,[12] in a report of fifty cases of myasthenia gravis in 1939, stated, "We have been unable to associate myasthenia gravis with enlargement of the thymus gland. All roentgen ray studies were negative for thymic enlargement. . ." Viets, in discussing a paper by Campbell, and associates[5] in 1941, reported finding roentgenographic evidence of thymus tumor in only one of eighty-five cases.

Fortunately, Dr. C. A. Good became interested in the roentgenologic aspects of the problem, and he undertook a study of all our cases of myasthenia gravis. It was found that in the majority of cases roentgenoscopy and roentgenograms

made with the patient in the lateral and oblique positions were necessary to demonstrate tumors (Figs. 8, *a* and *b*, and 9, *a* and *b*). In a series of 191 consecutive cases studied since 1941, our roentgenologists have made a definite diagnosis of tumor in the anterior part of the mediastinum in thirty cases, an incidence of 15.7 per cent. In two other cases, a tumor was suspected but evidence was not sufficient for a definite diagnosis to be made. It is obvious now that many thymic tumors have been overlooked in the past that might have been diagnosed by roentgenologic methods now practiced.

There is reason to believe that the aforementioned incidence of 15.7 per cent of thymic tumors in cases of myasthenia gravis found on roentgenologic examination now approaches the actual frequency of occurrence of this condition. Of the thirty aforementioned cases in which a definite roentgenologic diagnosis had been made, the diagnosis was verified surgically in seventeen cases and at necropsy in five cases. In eight cases the roentgenologic diagnosis remained unverified, but in these the roentgenographic evidence was unequivocal. Furthermore, in none of nineteen cases in this series in which the results of roentgenologic examination were negative for tumor have tumors been found at surgical exploration (eighteen cases) or at necropsy (one case). Only once in this series have roentgenologic observations been misleading. In one case a small tumor was diagnosed roentgenologically, but a tumor was not found at exploration. We believe that the incidence of 15.7 per cent for tumors found at roentgenologic examination approaches the true incidence of thymic tumors in myasthenia gravis. The higher incidences reported in the literature are based largely on reports of tumors found at necropsy, and since there is a natural tendency to report those cases of myasthenia gravis in which a tumor is found, figures based on such reports are not a true indication of the incidence of thymic tumor in myasthenia gravis.

The thymus gland has always puzzled pathologists, and thus far few definite conclusions can be reached regarding the pathology of the thymus in relation to myasthenia gravis. Microscopically, these tumors most closely resemble lymphosarcoma. However, Dr. McDonald, of the Section on Surgical Pathology, of the Mayo Clinic, after reviewing all the tumors we have removed surgically and those found at necropsy, has pointed out that the tumors are not true lymphosarcomas for three reasons. First, they do not respond to roentgen-ray therapy as a lymphosarcoma would be expected to do. For some patients, remission of symptoms has been obtained after deep roentgen-ray therapy, but there is not a consistent reduction in the size of the tumor. Second, there have been areas of calcification in some of these tumors, a condition never found in lymphosarcoma. Third, there is no evidence of any involvement of other lymph nodes in the body, such as would be expected if these lesions were lymphosarcomas. In some instances these tumors have been well encapsulated and easily removed. In other cases in which the tissues were almost identical microscopically to the tissue of encapsulated tumors, the tumor invaded the pleura, the lung, and even the large blood vessels in the mediastinum (in Fig. 10 are seen one thymoma projecting to the right at the level of the aortic arch, and another thymoma situated high in the anterior part of the mediastinum).

Fig. 8 *a*.—Posteroanterior roentgenogram of the thorax which shows no evidence of thymoma; *b*, lateral roentgenogram in the same case, showing (see arrows) a bilobate flat thymoma situated in the anterior part of the mediastinum, in close association with the base of the heart and with the aorta.

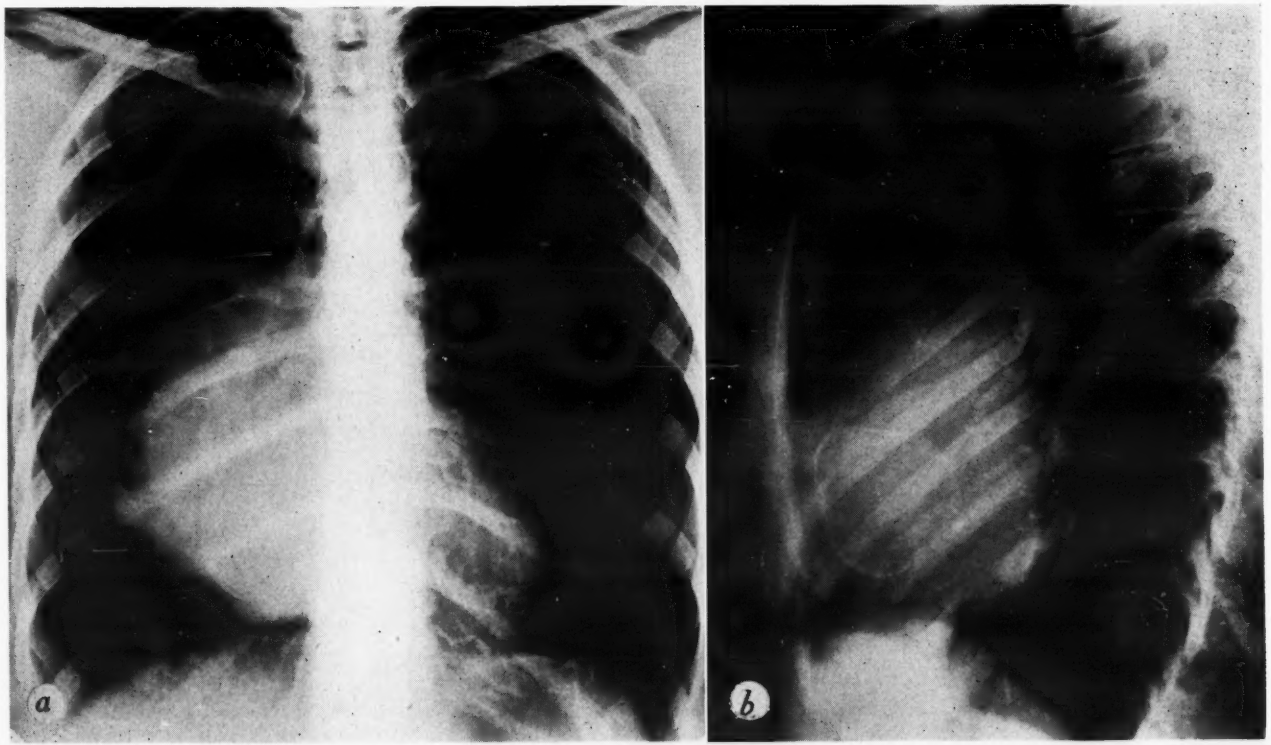

Fig. 9 *a*.—Large, rounded thymoma situated in the anterior part of the mediastinum and projecting to the right part; in the inferior portion of the mass is a cyst with calcified walls; *b*, lateral roentgenogram, same case.

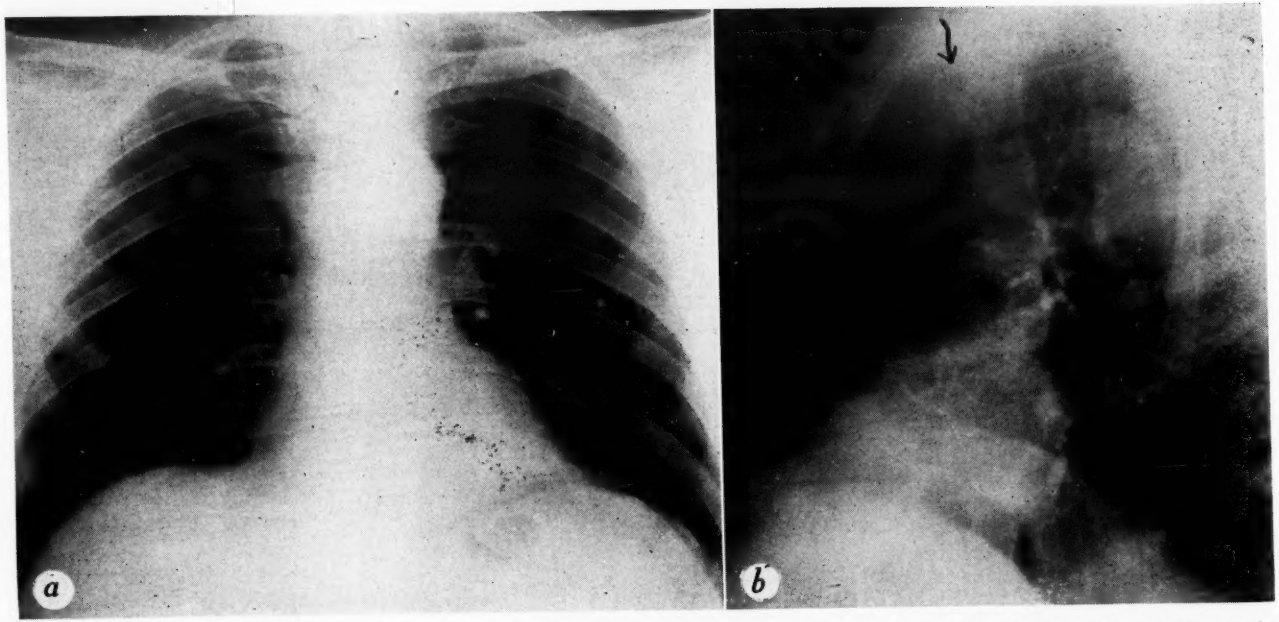

Fig. 10 *a*.—Thymoma projecting to the right at the level of the arch of the aorta; *b*, thymoma situated high in the anterior portion of the mediastinum (see arrow).

Strangely enough, in our experience, the tumor has not metastasized or spread outside the thoracic cage in any instance. In five patients it had been impossible to remove the tumor completely because of its extent and invasion. With deep roentgen therapy these patients have gotten along surprisingly well, as regards both their myasthenia gravis and evidence of recurrence or extension of their tumor. Microscopically, and also because of their invasive character, these tumors of the thymus gland appear to be malignant, yet their clinical course is not that which would be expected from a malignant lesion. For the present, we believe the term "thymoma" is the best name that can be applied to these lesions.

The hyperplastic thymus gland that has been removed from patients who have myasthenia gravis has not shown any remarkable pathologic characteristics. Microscopically, these glands are identical with the hyperplastic thymus glands of individuals suffering from hyperthyroidism.

It has been impossible, from our present experience, to establish any relationship between the pathology of the thymus gland found at operation and the severity of the myasthenia gravis, or to predict on the basis of the pathologic observations the benefit that might be expected from operation.

The role of roentgen therapy for these thymic tumors is of interest. Four patients had no roentgen therapy at any time, two had roentgen therapy before operation but none after, three had roentgen therapy after operation but none before, and six had roentgen therapy both before and after operation. It is difficult to evaluate just what effect this therapy has had on the tumors, but it is of interest to note that those patients in whom some tumor tissue remained and who received roentgen therapy are alive and getting along surprisingly well even in the presence of what had appeared at operation to be an invasive malignant lesion.

SUMMARY AND CONCLUSIONS

Our experience in a series of thirty-two patients with myasthenia gravis in which operation on the thymus gland was performed is reported. In fifteen patients tumors were found, and in seventeen there was no tumor. From our experience, we believe that thymectomy has been of value in the treatment of myasthenia gravis. The results to date warrant thymic exploration in all cases of myasthenia gravis in which the disease is severe or progressive and in which the patient's condition will permit consideration of surgery.

The sternum-splitting approach offers the best exposure in most instances. The risk of operation is not excessive, but the patients require the strictest vigilance and care in both the preoperative and postoperative management.

REFERENCES

1. Bell, E. T.: Tumors of the Thymus in Myasthenia Gravis, J. Nerv. & Ment. Dis. **45**: 130-143, 1917.
2. Blalock, Alfred: Tumors of the Thymic Region and Myasthenia Gravis, Am. J. Surg. **54**: 149-150, 1941.
3. Blalock, Alfred: Thymectomy in the Treatment of Myasthenia Gravis; Report of Twenty Cases, J. THORACIC SURG. **13**: 316-336, 1944.

4. Blalock, Alfred, Mason, M. F., Morgan, H. J., and Riven, S. S.: Myasthenia Gravis and Tumors of the Thymic Region; Report of a Case in Which the Tumor Was Removed, Ann. Surg. **110**: 544-560, 1939.
5. Campbell, Eldridge, Fradkin, N., and Lipetz, B.: Myaesthenia Gravis Treated by Removal of Thymic Tumor; report of two cases, Tr. Am. Neurol. A. **67**: 14-15, 1941.
6. Editorial: Myasthenia Gravis and the Thymus, Lancet **2**: 673-674, 1942.
7. Keynes, Geoffrey: The Surgery of the Thymus Gland, Brit. J. Surg. **33**: 201-214, 1946.
8. Miller, H. G.: Myasthenia Gravis and the Thymus Gland, Arch. Path. **29**: 212-219, 1940.
9. Norris, E. H.: The Thymoma and Thymic Hyperplasia in Myasthenia Gravis With Observations on the General Pathology, Am. J. Cancer **27**: 421-433, 1936.
10. Poer, D. H.: Effect of Removal of Malignant Thymic Tumor in a Case of Myasthenia Gravis, Ann. Surg. **115**: 586-593, 1942.
11. Sauerbruch: Quoted by Blalock, Alfred, Mason, M. F., Morgan, H. J., and Riven, S. S.[4]
12. Viets, H. R., and Schwab, R. S.: The Diagnosis and Treatment of Myasthenia Gravis; With Special Reference to the Use of Prostigmine, J. A. M. A. **113**: 559-562, 1939.
13. Weigert, Carl: Pathologisch-anatomischer Beitrag zur erb'schen Krankheit (Myasthenia gravis), Neurol. Centralbl. **20**: 597,601, 1901.

DISCUSSION

DR. ALFRED BLALOCK, Baltimore, Md.—It has been approximately five years since I performed the first total thymectomy in the treatment of myasthenia gravis. Von Haberer and others apparently thought they had been doing total thymectomies, but they used only an incision in the neck, and the entire thymus cannot be removed through this limited incision.

I hope that I learned a good lesson from our early experience with this disorder. In July, 1941, I performed two total thymectomies in bedridden patients who could not raise their heads off the pillow. These patients did very nicely following operation. One did not require prostigmine, beginning ten days after the operation. The other has not required prostigmine since twenty-one days following operation. I thought that we had an answer to this problem of the relationship of the thymus and myasthenia gravis, but such does not appear to be the case.

Two years ago I reported before this society the results in approximately twenty patients with myasthenia gravis who had had thymectomies. Dr. Clagett has listed those on one of his slides today. I would like to remark upon two of the patients in that group, one of whom was classified as being markedly improved, the other as slightly improved.

Both of these patients have died during this two-year period. I was particularly disappointed about the patient who was thought to be so markedly improved. This patient had had a thymic tumor, a total thymectomy was performed, and after a period of months prostigmine was no longer required. I had a telegram from her doctor in Fort Worth some six or eight months ago, saying that she was very ill with a respiratory infection, and wanted my advice. I advised a respirator, but the patient died despite this form of treatment. At autopsy, a thick piece of thymic tissue, about the size of the end of one's thumb, was found in a position where one would not expect to find thymic tissue at the time of operation.

The second patient, who was not much improved and who has died also from a severe respiratory infection, also had a piece of thymic tissue in a very abnormal position. So one could still say, if one cared to, that these patients succumbed because they still had some thymic tissue. That, I am afraid, is not the true story, and one thing that makes me think that, is that a year following the operation I lost a very eminent physician, Dr. Henry Dawson, of the Presbyterian Hospital, who had a small vascular thymic tumor. He appeared to be somewhat improved, not markedly, following the operation, but died a year following a complete thymectomy. The examination did not reveal any thymic tissue whatever.

It seems fairly definite that myasthenia is not totally dependent on an abnormality of the thymus gland. It also appears that one gets the best results in those patients following thymectomy who have had the disease process for the shortest period of time. That would indicate that this condition, if long continued, may lead to irreversibility. That is purely a supposition on my part.

I do hope that some one of us may perform thymectomies in patients with myasthenia gravis who have not had prostigmine. It may be that prostigmine is a poison of some sort,

and it may be that some of the poor results are explainable on the basis of prolonged prostigmine administration.

Another problem which I hope someone will work upon is one in which Dr. Henry Dawson, the late Dr. Dawson to whom I referred a moment ago, was particularly interested, and that was the working out of a method by which one could maintain the desired blood level of prostigmine, particularly in the postoperative period, because we have very little idea today as to how much of the oral prostigmine is used at any one time.

In concluding, after having said again that I have enjoyed this excellent paper by Dr. Clagett, I would like to say what is obvious to all of you, and that is that the thymus is located in a region in which all of us are particularly interested. As a matter of fact, if one counts the structures within the thoracic cavity, there are not many of them, and here is one that we know nothing whatever about. I think that there is little doubt, at least in my mind, that this structure doesn't just happen to be there. It is there for some purpose, and I am hoping some day that some person in this organization, and I think it will require one who has a good deal of special knowledge in chemistry or physiology, will throw some light on the function of the thymus.

DR. RALPH ADAMS, Boston, Mass.—Two years ago it was suggested that from time to time in these discussions we add the experience of various others than the essayists in this disease.

We have operated upon eight patients with myasthenia gravis, all without tumors. All, without exception, have been improved, some more in their own estimation than in ours. We have classified the results as follows: considerably improved, two; moderately improved, four; slightly improved, one, and dead three days after operation, one.

One patient had ceased prostigmine for three and a half years, and eight months ago had a recurrence of her difficulties. The prostigmine need has been reduced in most cases from one-half to two-thirds.

All patients whom we have operated upon have required preoperatively from a minimum of 90 mg. to a maximum of 360 mg. of prostigmine daily. All patients now require between 15 and 45 mg. a day.

The subjective improvement has frequently been greater than anticipated, and is believed to reflect only the influence of an optimistic psychologic attitude.

One death occurred postoperatively. Five of the other seven patients have returned to work.

I wonder if I may be allowed a little speculation along with Dr. Blalock. The clinical evidence of a relationship between the thymus and myasthenia gravis is established, but we certainly lack scientific proof of the type that can be established for thyroid hyperplasia and exophthalmic toxicity, or certain types of adrenal tumor and hypertension. Perhaps the thymus is the cause of the disease, but perhaps it is only one link in a chain of circumstances which we recognize as it weakens and eventually paralyzes and kills the patient.

In that connection, I would like to ask if anyone who has dealt with this disease surgically has encountered a case in which the disease developed postmenopausally. I have been interested to find that six of these eight patients were worse premenstrually. All of our cases were females.

There has been some recent work at the Women's Free Hospital in Boston and at the Harvard Medical School, indicating the presence of a very toxic substance in the menstrual secretions. We are all familiar with the improvement that often occurs in myasthenia gravis during pregnancy. I wonder if one might obtain a possible lead to the causation of this disease by examination of the menstrual secretions of myasthenia gravis patients for evidence of a curare-like effect in animals.

DR. ALTON OCHSNER, New Orleans, La.—Dr. Clagett, will you tell us if, in any of your patients, there was complicating hyperthyroidism?

A quarter of a century ago, the European surgeons were interested in thymic disease because of the relationship between the thymus and the thyroid. In our service at the Charity Hospital, we had a Negro patient, who had a severe hyperthyroidism and myasthenia

gravis. There have been relatively few cases reported, and they represent a dual problem. We thought that it was probably desirable to treat the hyperthyroidism first. A thyroidectomy was done, and at the time a large thymic tumor was found and, although it was probably poor judgment, we went ahead and took out the thymus, which is a hazardous procedure.

The patient got along very well, in spite of the fact that he was subjected to two major surgical procedures.

It has been the feeling of those individuals who have had such cases that the hyperthyroidism possibly nullifies some of the undesirable effects of the thymic hyperplasia. This patient did not have a tumor. It was enormous hyperplasia.

Whether our patient got along as well as he did because we did both procedures, the thyroidectomy and the thymectomy, at the same time, I don't know. I admit that was poor judgment, but it was tempting not to go ahead.

DR. R. H. SWEET, Boston, Mass.—I do not feel competent to discuss myasthenia gravis, but have been puzzled for a long time by this subject of thymic tumors. My experience in the field enters there, because I have seen an appreciable number of such tumors where there has been no connection whatever with this disease.

For example, in forty successive mediastinal tumors removed at our hospital in the last few years, twenty were solid tumors and four of those were thymomas. Two of the latter showed malignant changes. Then just to mention the other aspect of the situation, another patient recently observed, who had been seen for a number of years in our clinic with an anterior mediastinal tumor, developed symptoms of myasthenia gravis after a long period of observation, was operated upon, and died as a result of the operation.

DR. W. A. HUDSON, Detroit, Mich.—As a matter of record, I would like to mention a lady 52 years of age, who developed symptoms of myasthenia gravis within a year of the time that she was seen. She had had no previous special medication, neither had she had any prostigmine. She was subjected to surgery.

(Slide.) This reproduction of x-ray films shows, in an anteroposterior view, a mass protruding into the medio border of the upper lung field on the right and in the lateral view. This mass is seen to lie in the anterior mediastinum.

It is now four years since the lady was operated upon. She has been completely relieved of her symptoms. Whereas before she had given up her household duties, she has returned to the care of her home.

(Slide.) This slide represents the specimen itself, which is roughly horseshoe in shape. It had the appearance of thymic tissue, the mass weighing 152 Gm.

I think that it might answer one of the questions, if there have been any cases seen developing after menopause.

DR. O. T. CLAGETT, Rochester, Minn.—In regard to Dr. Ochsner's question on hyperthyroidism, the basal metabolism rates had been determined in all my cases before operation on the thymus. At the Clinic we have seen several patients who had hyperthyroidism and myasthenia gravis. I have not operated on the thymus of these patients yet. Dr. Pemberton has done thyroidectomy for hyperthyroidism on some patients who have had myasthenia gravis.

As far as Dr. Sweet's comments are concerned, we have encountered very few thymic tumors in persons who did not have myasthenia gravis, but undoubtedly they do occur.

We do have reason to think that some of our patients probably had thymic tumors before myasthenia gravis developed. Although we cannot definitely prove this, it seems entirely possible.

We have had several patients who developed myasthenia gravis after the age of 50 years and one who developed it at 70. So apparently the disease can occur at almost any age, regardless of menopause.

AEROSOL PENICILLIN AS A THERAPEUTIC ADJUNCT IN THE PREPARATION OF PATIENTS WITH SUPPURATION OF THE LUNG FOR PULMONARY RESECTION

CHARLES W. FINDLAY, JR., M.D., AND RICHARD H. SWEET, M.D.
BOSTON, MASS.

BRONCHIAL secretions in patients with pulmonary suppuration have often been a source of trouble at operation to both the surgeon and the anesthetist. The induction of anesthesia has frequently been difficult. Numerous aspirations of the trachea and bronchi during operation have delayed the surgical procedure, and in some instances death has occurred on the operating table due to the drowning of the patient in his own secretions.

Parenteral and oral chemotherapy have been of considerable value in preparing patients with bronchiectasis or lung abscess for surgery. At the Massachusetts General Hospital during recent years oral sulfadiazine and intramuscular penicillin have been given routinely before operation to patients with these conditions. The dosage and duration of administration have been those recommended in the current literature. In spite of this treatment, complications due to bronchial secretions during operation have continued.

In an attempt to decrease further these bronchopulmonary exudative processes, aerosol penicillin inhalations have been used preoperatively in this clinic for the past six months. The first twenty patients subjected to this treatment have been carefully studied to determine the efficacy of the inhalations and the criteria for predicting good anesthetic courses.

TECHNIQUE

Numerous articles have been written on aerosol penicillin therapy during the past year. Segal has written an excellent review of the subject with a complete bibliography.*

The apparatus selected was the simplest available which would be adequately effective and the easiest for the patient to manage. Oxygen was used to nebulize the drug. The control valve of the oxygen tank was usually set at 5 L. per minute and the gas was conveyed to a vaponephrin nebulizer by rubber tubing into which was inserted a glass Y tube. The aperture at the top of the nebulizer was left open and no mechanisms for condensing the expired air were used.

In most instances 50,000 units of sodium penicillin dissolved in 1 c.c. of isotonic saline solution were instilled in the nebulizer. A half-strength preparation of the drug was usually used for children. Unless the patient disliked the taste of peppermint, this flavor was added to the penicillin solution. Each 8 c.c. of penicillin solution contained 0.25 c.c. of a 20 per cent oil of peppermint solution in isopropyl alcohol.

From the surgical services of the Massachusetts General Hospital.
Received for publication Sept. 3, 1946.

*Segal, M. S.: Progress in Inhalation Therapy, Mod. Med. 14: 63, 1946.

The patient occluded the open side arm of the Y tube only during inspiration. He was instructed to breathe in slowly and deeply. At all other times the oxygen was diverted from the nebulizer via the open arm of the Y tube. The breath was held for five seconds after each inspiration. It usually took twenty minutes for the administration of one dose of penicillin.

The treatments were given eight times a day. Occasionally the 3 A.M. medication was omitted to give the subject six consecutive hours of sleep. The nebulizer was rinsed out with saline solution after each use. With a few exceptions the patient cooperated well and easily learned the routine of administration.

The type of pulmonary disease and the response to therapy determined the duration of the preoperative treatment. The average length of time for bronchiectatic patients was nine days. If the daily production of sputum did not decrease significantly at the end of this time, inhalation therapy was continued until a satisfactory response was obtained. It was found necessary to treat patients with lung abscess for long periods in order to reduce the sputum output.

Almost every patient with bronchiectasis or lung abscess requiring surgery has associated pneumonitis. It seemed important to treat this process in order to decrease its contributory effect on the volume of bronchial secretions as well as to increase the vital capacity. It has been emphasized that aerosol penicillin inhalations are designed primarily to combat local suppuration within the bronchi, and it is our impression that the pneumonitis is best treated systemically. Penicillin was given, therefore, intramuscularly and sulfadiazine orally to treat the parenchymal infection. The sulfadiazine was also given to control the abundant gram-negative organisms which usually appear in the sputum after aerosol penicillin has been given for a short time. Postural drainage was performed before the inhalation therapy was given.

CASES CHOSEN FOR THE TREATMENT

Fourteen patients with bronchiectasis were studied in this series. Their ages were between 9 and 59 years, but most of them were young adults. The majority had had signs and symptoms of this disease for most of their lives. All of them had had bronchograms made before treatment was instituted.

Three patients with lung abscess received penicillin inhalations prior to contemplated extirpative surgery. The disease was chronic in two cases and in the third the patient was a child whose signs and symptoms were of short duration. All three entered the hospital with significant temperature elevations due to undrained secretions or pneumonitis. Bronchoscopy showed evidence of bronchial obstruction in none, although severe bronchitis was always noted in the bronchial radicles leading to the diseased lobe.

Three cases of bronchogenic carcinoma with associated bronchitis, bronchiectasis, or cavitation were included in the series. One patient entered the hospital with a high temperature, while the other two showed no acute manifestations on admission. In no instance was a positive biopsy obtained by bronchoscopy. Two patients, however, were strongly suspected to have carcinoma, and aerosol

penicillin was given while they were awaiting surgery. The remaining patient was thought to have only suppuration and since he was acutely ill during the early hospital course, the duration of preoperative treatment was longer than is usual in a case of carcinoma.

Thirteen of the twenty patients produced more than 100 c.c. of sputum daily. Physical examination revealed considerable amounts of secretions in the trachea and bronchi of the three children who were studied. Because they swallowed the sputum, however, the amounts expectorated were not significant. Pulmonary resection of some type was contemplated in all but one.

RESULTS

As mentioned previously, the primary purpose of this study was to render surgical treatment safer by decreasing the bronchial secretions. Several other features were noted, however, which are important in evaluating the response to treatment. Most of these findings have been observed by other investigators.

Almost all of the patients volunteered the information that they felt generally improved after several days of aerosol treatment. This improvement was felt not only by those who were acutely ill on admission to the hospital, but also by those with chronic disease. It was most dramatic in patients with acute lung abscess, not included in this series, whose pulmonary lesions healed spontaneously. Some patients gained weight for the first time in many years.

The change in the symptom of cough was interesting to follow after penicillin inhalations were started. During the first two or three days many subjects coughed considerably while inhaling the aerosol, but usually no irritative phenomena were noted after this initial period and the coughing eventually decreased remarkably in both frequency and intensity. Two exceptions to this were noted in patients who were apparently sensitive to the peppermint flavoring. When this was omitted from the penicillin solution, treatments were continued without complaints. Two individuals with chronic bronchitis, emphysema, and histories of asthma, who were coughing considerably on admission to the hospital, continued to do so until operation (Cases 9 and 19). Two others whose secretions did not drain into the tracheas because of bronchial obstruction (Cases 17 and 18) also showed no decrease in coughing.

Three patients complained of substernal soreness, dry throat, or spasms of coughing after the inhalations were started. None of these disturbing features warranted discontinuation of the treatment, and they all disappeared after several days. The three children in this series appeared to perform the aerosol treatments as instructed, but they certainly did not understand completely the significance of this therapy. Two adults had difficulty in coordinating the different maneuvers outlined under Technique even after repeated instruction (Cases 3 and 19).

Gram-positive organisms were cultured from all sputa which were obtained before the inhalations were started. The sputa of seven patients yielded, in addition, gram-negative bacteria in the cultures. Penicillin-sensitivity examinations were not performed. Either during or at the end of treatment, gram-negative organisms predominated in the sputa of all but two patients. One of these

TABLE I

CASE NUMBER	AGE (IN YEARS)	DURATION OF AEROSOL PENICILLIN TREATMENT*† (IN DAYS)	DOSAGE AND DURATION OF PREOPERATIVE ORAL AND I.M. CHEMOTHERAPY	CHANGE OF DAILY SPUTUM OUTPUT (C.C.)	SPUTUM CULTURE BEFORE AEROSOL TREATMENT	SPUTUM CULTURE AFTER AEROSOL TREATMENT	COMPLICATIONS OF AEROSOL TREATMENT	OPERATION	ANESTHETIC COURSE	PATHOLOGIC FINDINGS
Bronchiectasis										
1	21	*15	Sulfadiazine p.o., 5 Gm. o.d. for 3 days	200 to 0	B. hem. str., Staph. albus	B. coli	Throat irritation from peppermint flavor	R.L.L. lobectomy	Uncomplicated	Atelectasis, chronic pneumonitis, saccular bronchiectasis
2	31	†10	Sulfadiazine p.o., 5 Gm. o.d. for 4 days; penicillin I.M., 16,000 U. q. 3 h. for 10 days	30 to 7	B. hem. Str., Pneumo. type 33	B. coli	None	L.U.L. lobectomy	Uncomplicated	Atelectasis, severe pneumonitis, saccular bronchiectasis, abscess formation
3	30	*12	Sulfadiazine p.o., 5 Gm. o.d. for 3 days	Never more than 10; patient swallowed sputum	B. hem. Str.	B. coli, Staph albus	Substernal soreness, intermittent treatment due to poor cooperation	R.M.L. & R.L.L. lobectomies	Difficult induction and course, aspirated 3 times	Atelectasis, chronic pneumonitis, saccular bronchiectasis
4	35	†12	Sulfadiazine p.o., 6.0 Gm. for 4 days; penicillin I.M., 24,000 U. q. 3 h. for 12 days	180 to 10	B. hem. Str.	B. coli	None	L.L.L. lobectomy and lingulectomy of L.U.L.	Uncomplicated	Atelectasis, chronic pneumonitis, saccular bronchiectasis

*Aerosol penicillin, 50,000 units, every three hours.
†Aerosol penicillin, 25,000 units, every three hours.
I.M., intramuscular.
p.o., by mouth.
o.d., daily.
u., units.
R.U.L., right upper lobe.
R.M.L., right middle lobe.
R.L.L., right lower lobe.
L.U.L., left upper lobe.
L.L.L., left lower lobe.

5	32	*8	Penicillin I.M., 12,000 U. q. 3 h. for 7 days	120 to 0	Staph albus	B. coli	None	L.L.L. lobectomy	Uncomplicated	Atelectasis, chronic pneumonitis, tubular bronchiectasis
6	23	*9		240 to 30	None taken	B. coli	None	L.L.L. lobectomy	Uncomplicated	Atelectasis, saccular bronchiectasis
7	20	*9	Sulfadiazine p.o., 4 Gm. o.d. for 3 days; penicillin I.M., 12,000 U. q. 3 h. for 12 days	120 to 60	None taken	B. coli, Staph. aureus	None	L.L.L. lobectomy and lingulectomy of L.U.L.	Uncomplicated	Atelectasis, saccular bronchiectasis
8	24	*9	Sulfadiazine p.o., 6 Gm. o.d. for 2 days	150 to 0	B. & a. hem. Str., H. influenza	B. coli, H. influenza	None	L.L.L. lobectomy and lingulectomy of L.U.L.	Uncomplicated	Tubular bronchiectasis
9	59	*15	Sulfadiazine p.o., 6 Gm. for 6 days	90 to 45	a. hem. Str., B. coli	B. coli	Considerable coughing throughout treatment	R.L.L. lobectomy	Uncomplicated	Segmental atelectasis and emphysema, pneumonitis, saccular bronchiectasis
10	10	†7	Sulfadiazine p.o., 3 Gm. o.d. for 3 days, penicillin I.M., 12,000 U. q. 3 h. for 7 days	Patient swallowed sputum	B. hem. Str., H. influenza, Pneumos.	B. coli	None	L.L.L. lobectomy	Easy induction, tracheal aspiration 4 times	Atelectasis, chronic pneumonitis, saccular bronchiectasis
11	53	*4	Sulfadiazine p.o., 6 Gm. o.d. for 3 days; penicillin I.M., 12,000 U. q. 3 h. for 6 days	60 to 30	Pneumos type 31	Staph. Albus, B. coli, B. proteus	None	L.L.L. lobectomy and lingulectomy of L.U.L.	Uncomplicated	Chronic pneumonitis, saccular bronchiectasis

TABLE I—CONT'D

CASE NUMBER	AGE (IN YEARS)	DURATION OF AEROSOL PENICILLIN TREATMENT*† (IN DAYS)	DOSAGE AND DURATION OF PREOPERATIVE ORAL AND I.M. CHEMOTHERAPY	CHANGE OF DAILY SPUTUM OUTPUT (C.C.)	SPUTUM CULTURE BEFORE AEROSOL TREATMENT	SPUTUM CULTURE AFTER AEROSOL TREATMENT	COMPLICATIONS OF AEROSOL TREATMENT	OPERATION	ANESTHETIC COURSE	PATHOLOGIC FINDINGS
12	22	*10		120 to 30	B. hem. Str., B. coli	B. coli	None	L.L.L. lobectomy and lingulectomy	Uncomplicated	Chronic pneumonitis, saccular bronchiectasis
13	23	*7	Penicillin I.M., 16,000 U. q. 3 h. for 2 days	150 to 90	B. & a. hem. Str.	B. coli	Not fully benefited due to faulty instruction	Resection of dorsal division of L.L.L. and lingulectomy of L.U.L.	Easy induction, tracheal aspiration 11 times	Acute and chronic pneumonitis, tubular bronchiectasis
14	9	*5	Sulfadiazine p.o., 3 Gm. o.d. for 2 days; penicillin I.M., 12,000 U. q. 3 h. for 5 days	Patient swallowed sputum	B. hem. Str.	B. coli	None	R.U.L. & R.M.L. lobectomies	Uncomplicated	Atelectasis R.M.L., saccular bronchiectasis
Lung Abscess										
15	60	†18	Sulfadiazine p.o., 6 Gm. o.d. for 3 days	180 to 45	B. hem. Str.	B. coli	Sore, dry throat during first week of treatment	R.U.L. lobectomy	Uncomplicated	Chronic pneumonitis, abscess cavity

16	8	†7	Sulfadiazine p.o., 6 Gm. o.d.; penicillin I.M., 16,000 U. q. 3 h., both for 12 days	Patient swallowed sputum	B. & a. hem. Str., B. coli	a. hem. Str.	None	Stormy induction, pulmonary resection postponed		
17	43	†10 *11	Sulfadiazine p.o., 6 Gm. o.d. for 17 days	240 to 45	B. & a. hem. Str., B. coli, Staph. albus	B. coli	Substernal soreness and coughing	R.L.L. lobectomy	Easy induction, aspiration twice	Chronic pneumonitis, bronchiectasis, abscess cavity
Bronchogenic Carcinoma										
18	54	*27	Penicillin I.M., 24,000 U. q. 3 h. for 17 days	150 to 60	B. & a. hem. Str., H. influenza	B. coli	Persistent cough	Rt. pneumonectomy	Uncomplicated	Atelectasis and bronchiectasis due to bronchial obstruction by carcinoma
19	66	*7	Penicillin I.M., 16,000 U. q. 3 h. for 7 days	100 to 15	B. & a. hem. Str.	B. coli	Difficult for patient to perform treatment properly	R.U.L. & R.M.L. lobectomies	Uncomplicated	Excavated carcinoma of R.M.L., emphysema of R.U.L., incomplete fissure between R.M.L. and R.U.L.
20	64	†8	Sulfadiazine p.o., 4 Gm. o.d., penicillin I.M., 24,000 U. q. 3 h., both for 3 days	270 to 60		Staph. albus	None	L. pneumonectomy	Uncomplicated	Atelectasis L.U.L., emphysema L.L.L.; occlusion of L.U.L. bronchus by carcinoma

exceptions occurred in a child with an unevacuated lung abscess (Case 16), the other in an adult with carcinoma obstructing a major bronchus (Case 20). *Bacillus coli* was the most common post-treatment organism found. Both gram-positive and gram-negative bacteria were cultured from the sputa of three individuals at the completion of the aerosol treatment. One of these was treated for only four days (Case 11). The second was so uncooperative that the treatment probably was not effective (Case 3). The third patient received adequate therapy according to our criteria (Case 7). It usually required four days of this regimen to eliminate gram-positive organisms from the sputum. Penicillinase was not used in the bacteriologic surveys, but the use of this enzyme in subsequent studies has not appreciably changed the results. Only fresh morning specimens of sputa were submitted for culturing purposes.

The change in the character and the amount of the sputum was striking. When the bronchial secretions were foul, aerosol therapy eventually eliminated the odor in every instance. Treatment also caused thinning of the sputum in most cases. Many times the patients volunteered this information and remarked that it was easier to cough up the secretions. The sputum production was significantly reduced in those individuals whose daily output was over 100 c.c. before entry. Often the volume of bronchial secretions increased during the first several days of inhalation therapy and then rapidly decreased. On one occasion the sputum output rose from 90 to 240 c.c. and ultimately diminished to 45 c.c. a day. The conversion of the bacterial flora in the sputum preceded its reduction in volume by one to three days in bronchiectatic patients. This interval was longer in those with lung abscess.

The anesthetic course at operation was uncomplicated in all but five instances. The term uncomplicated means that no difficulties due to bronchial secretions were encountered during induction and that tracheal aspiration of secretions was not necessary more than once in each patient. Standard doses of atropine and opium derivatives were given before operation. Two bronchiectatic subjects who were troublesome to the anesthetist were not adequately treated preoperatively (Cases 3 and 13). A child with bronchiectasis who appeared to be adequately treated required tracheal aspiration four times (Case 10). In one lung abscess case suction was necessary twice following the initial manipulation of the diseased lobe (Case 17).

The outstanding failure in this series occurred in a child with lung abscess who was scheduled for lobectomy (Case 16). He was considered to be well prepared for operation. Shortly after the induction of anesthesia, however, he practically suffocated in his own secretions and the intended procedure had to be abandoned. One month later the diseased lobe was removed. At this time the anesthetic course was again stormy but not as hazardous as on the first attempt.

On almost all occasions the anesthetists commented on the absence of bronchial secretions. They volunteered that in their experiences the patients treated preoperatively with aerosol penicillin for bronchopulmonary suppuration presented fewer anesthetic difficulties than those who had not been prepared in this way.

The immediate postoperative period was uneventful when the diseased lung tissue had been removed. It was only after forty-eight hours that complications appeared. In the bronchiectasis group, six patients developed atelectasis requiring bronchoscopic treatment between the second and third days following operation (Cases 2, 3, 4, 12, 13, and 14). In one case there was atelectasis which cleared spontaneously after a mucous plug was coughed up (Case 8). In each instance the pulmonary collapse occurred on the side operated upon. Another patient had bronchopneumonia eight days postoperatively (Case 6). Type III pneumococci were cultured from his sputum. Six bronchiectatic patients had no difficulties following surgery.

With one exception, the patients with lung abscess and carcinoma, on whom resections were performed, had benign postoperative courses. The one death in this series occurred in a patient whose right upper and middle lobes were removed for bronchogenic carcinoma (Case 19). For several days following operation, copious secretions in the trachea and bronchi required frequent aspirations. He died suddenly on the tenth postoperative day. The cause of death was undetermined.

The treatment after surgery was for the most part symptomatic. Aerosol penicillin was not given, although oral sulfadiazine and intramuscular penicillin were administered to one-half the patients. The remainder received only intramuscular penicillin. The postoperative chemotherapy was continued usually for one week. Empyema did not occur in any instance.

DISCUSSION

In this small series of cases the decrease in the amount of sputum production was the most important factor in obtaining a good anesthetic course. It was found that the daily record of the amount of sputum expectorated was the best index of the patient's preoperative status. This survey showed that an adult patient was a good operative risk if he had no sputum following aerosol therapy or if after two weeks of treatment the amount of production was decreased significantly to a small volume which remained constant.

An attempt was made to correlate the pathologic findings with the response to treatment. The sputa of patients with uncomplicated tubular bronchiectasis decreased in amount the most rapidly. The presence of saccular bronchiectasis or an abscess cavity required aerosol therapy for a longer period to obtain good results. Associated bronchial obstruction and atelectasis necessitated the longest treatment periods before the sputum was significantly reduced.

As might be expected, the lessening of the sputum eventually decreased the coughing. Another factor which contributed to the improvement of cough was the ultimate reduction of bronchitis in these patients. Almost all of them were bronchoscoped before penicillin inhalations were started and invariably marked inflammation of the bronchial mucosa was noted. When the fresh pathologic specimens were examined, however, inflammatory changes in the mucosa of the major bronchi were minimal in adequately treated patients.

In patients with bronchogenic carcinoma the preoperative period should not be prolonged in the hope of obtaining ideal results in the reduction of the sputum

output. If the amount of bronchial secretions is considerable, however, inhalations of aerosol penicillin may be of value while diagnostic procedures are in progress and while the patient is waiting to be scheduled for surgery.

The importance of concomitant therapeutic measures in the preoperative preparation should not be disregarded. Postural drainage, bed rest, and raising the blood proteins and hemoglobin to normal levels are of definite value. If there is associated acute or chronic pneumonitis, the use of intramuscular penicillin is important. Sulfadiazine should be used to control the obvious penicillin-resistant organisms in the sputum.

Individuation of the treatment is extremely important if a good preoperative preparation and a smooth anesthetic course are desired. It is necessary first to evaluate the pathology fully so that the duration and type of treatment can be tentatively prognosticated and outlined. When the inhalation therapy has been started, a careful check on the daily output and the bacterial flora of the sputum will indicate the response of the patient to treatment. The decrease of coughing and the improvement of general health are also worth noting. The habits of children, such as sputum swallowing and lack of expression as to general health, prevent satisfactory evaluation of their response to treatment. It is also difficult to be certain that they take the inhalation therapy efficaciously and seriously on every occasion. They are probably not suitable candidates for the aerosol treatment outlined here. On the other hand, the adults in this small and preliminary series of cases, who received adequate courses of aerosol inhalations, uniformly had minimal or no bronchial secretions at operation and the anesthetic courses were without complications.

ANESTHESIA FOR THORACIC SURGERY IN THE UNITED STATES ARMY

LIEUTENANT COLONEL LLOYD H. MOUSEL,* MEDICAL CORPS,
ARMY OF THE UNITED STATES

THE results obtained in seven thoracic surgical centers in the United States during World War II reflect the advances made in the field of anesthesia in relationship to the altered physiologic conditions of the open chest. During World War I many emergency thoracic surgical procedures were carried out and at that time it was determined by the end result that most procedures were dependent largely upon the anesthesia. It was obvious that many patients died during or soon after operation due to collapse of pulmonary tissue and paradoxical respiration during major operative procedures. The anesthesia equipment available during the years 1914 to 1918 was, in most instances, inadequate for thoracic surgical anesthesia. Nitrous oxide and oxygen were the agents used most often, although in some instances the anesthetist was forced to resort to the use of open drop ether. Methods were devised for the administration of intermittent positive pressure but these means were not particularly satisfactory. The carbon dioxide absorption method of anesthesia had not yet been developed. The high flow of gases necessary to maintain positive pressure without the accumulation of a dangerous amount of carbon dioxide proved extremely wasteful of anesthetic gases. Following the development of the carbon dioxide absorption method of anesthesia with rebreathing of anesthetic gases, equipment became available which has been in most instances quite satisfactory for the maintenance of anesthesia during open thoracotomy.

Prior to 1940 very little had been written on the subject of anesthesia for thoracic surgery. During 1940, Phillips, Livingstone and Engel[8] reported the anesthetic results in over 500 thoracic surgical operations. Ethylene oxygen anesthesia was used in 73.2 per cent of all thoracic operations. Eight of their patients developed severe shock on the operating table and were treated by means of blood transfusions. Preoperative transfusions were given to three patients at the beginning of operation. Eight patients were given blood the same day as operation. Less than 10 per cent of all patients received blood later. Postoperative oxygen therapy was required in only ten instances. Pneumonectomies were done under ordinary mask anesthesia without the use of endotracheal tubes. Eleven lobectomies were carried out without the use of either face masks or endotracheal tubes. The authors stated that positive pressure mask anesthesia was used only once and was seldom required.

In 1940, Beecher[1] recommended the use of ether and oxygen as the anesthetic of choice in major thoracic surgery patients. He stated that oxygen must be available in high concentrations because of reduced vital capacity and that ether allows more oxygen to be used than can be used with cyclopropane.

Received for publication Aug. 29, 1946.

*Now Clinical Professor of Anesthesiology, George Washington University, Washington, D. C.

He further stated that cyclopropane may interfere with oxygen uptake in the cells and that this agent has a toxic effect upon the heart in a relatively high percentage of patients. Whether toxic cardiac effects are responsible or not, the mortality rate seemed to be higher if cyclopropane was used than if ether was used as the anesthetic agent. He also condemned the use of avertin with nitrous oxide for thoracic surgical patients. Beecher stated that positive pressure is necessary at times in some cases and almost constantly in others so that endotracheal intubation is important. He condemned the use of inflatable cuffs, stating that they are not necessary and may cause severe irritation of the trachea. He also stated that controlled respiration is neither necessary nor advisable and that the production of respiratory failure removes the greatest safeguard against overdose. He stresses the importance of simplicity in anesthesia.

Wiggin and Schultz,[10] in 1941, recommended the use of cyclopropane in major thoracic surgery, although at times procaine infiltration was used in combination with the inhalation agents. Endotracheal catheters with inflatable cuffs were used routinely for lobectomy and pneumonectomy, without untoward effects from either intubation or pressure from the inflated cuff. Positive pressure administration was resorted to only when indicated.

Phillips, Livingstone, and Adams,[7] in 1941, stated that they seldom used endotracheal anesthesia because of the desire to avoid trauma of the tracheobronchial tree. Ethylene and oxygen were used in the majority of cases. Supplemental ether was avoided as much as possible because of increased irritation of the respiratory tract. All agents which inhibit the cough reflex were avoided if possible. They stated that operations on the heart, pericardium, and mediastinum may be successfully performed under local anesthesia.

Moyer,[4] in 1941, condemned the use of pentothal sodium and evipal soluble with simultaneous administration of a high concentration of oxygen. He found that in experimental animals, the barbiturates caused the response to 12 per cent carbon dioxide to change from an intense stimulation of breathing to a very minor stimulation, followed by serious depression of respiration as shown by cessation of respiration and asphyxial rise in blood pressure. Breathing during moderate evipal or pentothal anesthesia is likely to be largely and even entirely dependent upon reflex drives for maintenance. Any reduction of these reflex drives is apt to result in respiratory failure as is shown by changing from room air to oxygen during deep anesthesia. Dogs whose respiration was not greatly depressed while breathing room air showed a slowing of respiration and finally complete cessation following the administration of oxygen.

Nosworthy,[6] in 1941, advocated the use of controlled respiration. He brought about control by depressing the respiratory center with sedatives and anesthetic drugs. He advocated the use of one lung anesthesia for pneumonectomy. This he obtains by means of an endotracheal airway with bronchial tamponage on the affected side or by endotracheal intubation on the sound side. He is convinced that all thoracic surgery should be done under anesthesia deep enough to abolish all reflexes since coughing may tend to spread

the infection. He stated that chest patients commonly have a low vital capacity and the lateral position on the operating table handicaps them still further. Therefore, the anesthetic technique should make use of all alveolar membrane for gaseous exchange and permit a high oxygen concentration. He stated that controlled respiration with ether or cyclopropane fulfills this requirement. "Paradoxical respirations will at times develop under local anesthesia for thoracoplasty and have been a common cause of death in the past, especially if too many ribs were removed at a single operation." The lung on the sound side discharges part of its contents into the collapsed lung. The to-and-fro movement of air makes the movements of the lung on the affected side paradoxical since it expands with expiration and collapses with inspiration. Nosworthy also stated that the anesthetist must be prepared to supervise continuous circulatory resuscitation and, second, he must make sure that efficient respiration is taking place. He must not wait for signs of circulatory depression to develop but must institute resuscitative measures early. He advocated a constant drip transfusion during all thoracoplasties.

Neff and associates[5] recommended the use of cyclopropane for pneumonectomy and lobectomy. Small doses of premedication were used. Apnea was produced by overventilating the patient's lungs through a canister of soda lime. Controlled respiration was maintained throughout the course of operation. They reported a hospital death rate of 10.5 per cent following pneumonectomy and 6.6 per cent following lobectomy.

In 1940, Beecher advocated positive pressure anesthesia and did not find a rise in blood carbon dioxide. He disapproved of rhythmic ventilation or controlled respiration on the grounds that with the abolition of active breathing, the anesthetist lost his chief guide to the depth of anesthesia.

Randolph and Kober[9] in 1943, reported 123 thoracoplasties done satisfactorily under pentothal anesthesia.

Esten[3] stated that although the cough mechanism has a supposedly spreading action, the incidence of spread of infection in patients with a cough reflex prior to surgery is extremely low. He stated that spontaneous respirations, if allowed to persist, result in increased oxygen demand, exhaustion of the respiratory muscles, and a diminished elimination of carbon dioxide, and that the to-and-fro canister is a more efficient carbon dioxide absorber giving less resistance than the circle type filter. He further stated that positive pressure anesthesia interferes with the bellows action of the lungs and the mixing of the gases. The elimination of carbon dioxide from the alveolar spaces is entirely dependent upon this mixing action. An increase of carbon dioxide, without notable clinical signs, may occur.

Bourne and co-workers[2] recommended the use of nupercaine spinal anesthesia for thoracic surgery. He reported an anesthetic death rate of 3.9 per cent.

During the recent war years, seven thoracic surgical centers* were set up in the United States for the purpose of providing the best possible care for

*One center was closed in 1944.

soldiers who required surgery of the chest. These centers were organized in such a way that the personnel originally selected to staff these institutions were able to remain in most instances throughout the duration of the war. In this way, surgical and anesthesia teams were formed and, in their close cooperation over a long period of time, became intimately associated in their common problems. Close cooperation of all personnel was to a large extent responsible for the low mortality figures reported here. All types of surgical conditions pertaining to diseases of the thorax were treated in these centers. However, this paper deals only with that group which gives rise to the major anesthetic problems, namely, lobectomy, pneumonectomy, and mediastinal tumor.

By Dec. 1, 1945, 559 lobectomies had been reported. A 1.9 per cent over-all mortality rate was reported in this series of cases. Three of the deaths were definitely related to anesthesia. One of the patients died immediately after surgery and following the aspiration of a large amount of vomitus into the tracheobronchial tree. The second died approximately one hour after operation, due to cerebral anoxia. This patient developed profound shock during surgery and the treatment of shock was delayed because of the difficulty in administering whole blood. The third patient died twenty-four hours after operation due to inability to obtain complete oxygenation during the last part of surgery. This death probably could have been prevented by early complete bronchoscopic aspiration during the operation.

There were 109 mediastinal tumors. Of this group, eighty-three tumors were removed and exploration was carried out in twenty-six patients for biopsy diagnosis. In this series, one patient died, giving a 0.9 per cent over-all mortality rate. This patient died as the result of cerebral anoxia on the third postoperative day. Massive hemorrhage occurred during the operation, the patient became pulseless and blood pressure was unobtainable. The condition was relieved by massive blood transfusion but anoxia had apparently been sufficient to cause irreparable damage to the higher centers.

In the series of pneumonectomies carried out in our thoracic surgical centers eight deaths could be associated with anesthesia, four of them being definitely anesthetic deaths. Two patients were reported as having died from cardiac failure and two were found to have died of obstruction of the main stem bronchus on the unoperated side. Four of the patients died of pulmonary edema,* one eight hours, two twenty-four hours, and one seventy-two hours postoperatively. In all four of these patients, large amounts of fluid, consisting of blood, plasma, and saline, had been given on the operating table, and during the first few hours postoperatively.

Of the patients reported in this entire series, all operations were done under endotracheal anesthesia. During the early part of the war a few patients were anesthetized with cyclopropane. However, well over 95 per cent of the patients reported on were anesthetized with nitrous oxide, oxygen and ether with ether and oxygen maintenance. No serious complications were reported following

*These cases were reported as being related to anesthesia because it is thought to be the responsibility of the anesthetist to prevent shock by replacing all blood loss, as it occurs, with whole blood.

the use of endotracheal tubes. In approximately 80 per cent of all endotracheal procedures, an inflatable cuff was used to insure a completely tight airway. In approximately 20 per cent, no cuff was used. A face mask was placed directly over the endotracheal airway in order that a tight seal could be obtained.

In five centers, intermittent positive pressure anesthesia was used. In two centers, the apneic technique of controlled respiration was practiced routinely. The over-all anesthetic mortality study leaves room for conjecture regarding the wisdom of using controlled anesthesia. All deaths related to anesthesia occurred in centers where the apneic technique of controlled respiration was used routinely for lobectomies, pneumonectomies, and removal of mediastinal tumors.

In the study of the over-all mortality figures, several pertinent points become obvious. In the first place, the anesthesia has been relatively simple but it has been carried out by men who have been extremely interested in the subject of anesthesia for thoracic surgery and have given their personal attention to these patients. I have been impressed with the fact that the more toxic anesthetic agents have not been used to any great extent and that by far the large percentage of patients were not carried on the apneic technique as has been suggested by some writers. Careful observation of all patients on the operating table with the prevention or early relief of tracheobronchial obstruction, prevention of anoxia, and prevention of shock by adequate replacement of blood as hemorrhage occurs has been responsible for this excellent record.

Major thoracic surgical procedures can be carried out successfully using the closed method of ether-oxygen administration through a circle type of filter. Postural drainage immediately before induction will minimize the amount of foreign material in the tracheobronchial tree of patients suffering from suppurative disease of the lung. Bronchoscopic aspiration immediately before operation may cause hemorrhage into the tracheobronchial tree. Patients usually become somewhat apprehensive during and immediately following bronchoscopy, making them unfit subjects for smooth anesthetic induction. It is my belief that bronchoscopic aspiration should not be carried out immediately before surgery in the elective case. Conservative amounts of premedication are administered to these patients approximately two hours before operation.

The primary anesthetic induction is carried out using 80 per cent nitrous oxide and 20 per cent oxygen. After the patient's reflexes have been dulled by the action of nitrous oxide, ether is gradually added to the system and the administration of nitrous oxide is discontinued. Endotracheal intubation with a McGill endotracheal catheter equipped with an inflatable cuff is now carried out. The endotracheal catheter is connected directly to the anesthesia machine and the equipment carefully checked to assure a completely leakproof system. The patient is placed in position on the operating table in such a manner as to assure maximum respiratory excursion. Sandbags under the dependent portion of the chest or breaking of the operating table in such a manner as to interfere with respiratory excursion should be avoided. A large bore needle is placed into a convenient vein and a very slow drip of whole blood is started be-

fore sterile drapes have been put in place. It is essential in all major thoracic surgical procedures to prevent the onset of shock. This can be done by an accurate estimation of blood loss and the replacement of such loss as it occurs. If blood loss is not replaced as it occurs, the patient may go into a state of shock which will necessitate the administration of large quantities of fluids postoperatively, resulting in some instances in pulmonary edema.

The tracheobronchial tree is aspirated frequently, using a soft rubber urethral catheter in order to prevent tracheobronchial obstruction. These patients are carried without positive pressure in the anesthesia machine until a few minutes before the pleura is opened. Approximately two or three minutes before the pleural cavity is entered, positive pressure of approximately 8 cm. of water is built up in the system in order to prevent a sudden collapse of the lung following the opening of the pleura. Positive pressure is gradually reduced over a period of five or six minutes' time, allowing the lung to collapse slowly. If this technique is carried out, paradoxical respiration will rarely develop. Should interference with respiratory excursion develop after the lung has been deflated, enough positive pressure is added to control the mediastinal shift. This amount of pressure will rarely exceed 5 cm. of water. Occasionally the patient will be encountered in whom a slight amount of positive pressure will be required throughout the duration of surgery, but these cases are rare. Most patients will develop a stable mediastinum provided initial decompression of the lung is carried out slowly. These patients will rarely require positive pressure to maintain adequate pulmonary and cardiovascular circulation. If the lung is allowed to collapse completely the surgeon may carry out his work without the interference of an inflated lung protruding into the wound.

It has been found on measurement of the tidal volume of thoracic surgical patients, that the average case of open pneumothorax, where one complete lung is collapsed, is between 400 and 500 c.c. The color of these patients remains good. The normal blood pressure and pulse rate would indicate that anoxia does not exist. In cases of lobectomy, it is believed that reinflation of the uninvolved lung tissue on the side operated upon should be carried out every twenty to thirty minutes. This procedure probably minimizes the danger of postoperative atelectasis and may prevent unintentional ligation of a bronchus in the uninvolved lobe. Tracheobronchial aspiration must be carried out at frequent intervals with a catheter long enough to reach the terminal portion of the tracheobronchial tree. One must not wait until mucus can be heard in the airway before carrying out aspiration. It is possible for a large amount of foreign material to gravitate from the diseased lung to the contralateral side, producing partial or complete obstruction without changes in the audible tone of respiration.

If the patient is draped in such a manner that the anesthetist can see into the chest at all times, bronchial obstruction can be detected frequently by noting increased diaphragmatic movements several minutes before clinical symptoms of anoxia can be recognized from the color of the patient or from changes in pulse and respiration. It is essential that the anesthetist be alert at all times

in order that instantaneous diagnosis of complications may be made and corrective measures instituted at once. Otherwise, tracheobronchial obstruction may terminate in death on the operating table or death from cerebral anoxia several hours or days postoperatively. Rarely is there reason for carrying these patients on controlled respiration.

At the termination of operation, a sufficient amount of positive pressure is gradually built up in the machine to reinflate the remaining lung tissue. This pressure is maintained until the chest wall has been completely closed in order to avoid the possibility of pneumothorax. At the time of chest wall closure, pulse and blood pressure must be watched carefully, for occasionally the pressure required for re-expanding the lung will be great enough to interfere with return of circulation to the heart once the chest wall is closed. If increased pulse rate and decrease in blood pressure takes place soon after the chest wall has been closed, positive pressure in the anesthesia system must be reduced at once.

It has been the policy in most thoracic surgical centers in the Zone of the Interior to carry out routine bronchoscopic procedures immediately after the operation and before the patient is returned to his room. If an x-ray is made of the patient's chest at this time, conditions such as atelectasis, pneumothorax, or hemothorax can be detected and corrective measures taken immediately. It is believed that if this routine is adopted by all thoracic surgical clinics, many serious postoperative complications can be avoided. If pulmonary edema is to be avoided, great care must be exercised in the administration of fluids during operation and in the immediate postoperative period. Mortality figures impress us with the necessity of extreme caution in fluid therapy, particularly during and following pneumonectomy. The average patient undergoing lobectomy seems to tolerate rather large quantities of intravenous fluids without difficulty. However, slight overloading of the circulation with intravenous fluids during and following pneumonectomy is apt to produce fatal pulmonary edema. If on-the-spot replacement therapy using whole blood is carried out during operation, there is usually little need for large quantities of intravenous fluids postoperatively in an attempt to elevate a seriously reduced blood pressure.

I am impressed with the low mortality and morbidity figures following the use of ether in major thoracic surgical cases, particularly in the group of patients suffering from suppurative disease of the lung, for it is in this group that many writers have condemned the use of ether because of its irritating qualities.

CONCLUSIONS

1. Ether is a safe anesthetic agent when used in a closed system with a high concentration of oxygen in major thoracic surgical procedures.

2. Endotracheal catheters are essential for the maintenance of a clear airway for frequent tracheobronchial aspiration and for the administration of positive pressure when indicated. The use of endotracheal catheters and inflatable cuffs have produced no harmful effects in this series of patients.

3. Continuous positive pressure anesthesia is not required in most patients. Intermittent positive pressure is essential.

4. Intermittent positive pressure anesthesia and the method of controlled respiration have both been carried out in a large series of major thoracic surgical procedures.

5. All deaths related to anesthesia occurred in centers where controlled respiration was carried out routinely during anesthesia.

6. Re-expansion of collapsed pulmonary tissue for the purpose of preventing pneumothorax can be safely carried out using measured positive pressure at the termination of the operation.

7. Uninvolved lung tissue should be re-expanded frequently during the course of operation in an attempt to minimize the dangers of postoperative atelectasis and to assist the surgeon in locating lines of demarcation.

8. Care must be exercised in the administration of large amounts of fluids during operation and during the immediate postoperative period.

9. On-the-spot replacement therapy using whole blood will prevent the onset of shock in most instances.

10. Patients undergoing pneumonectomy are apt to develop fatal pulmonary edema if excessive quantities of fluids are given intravenously.

11. Immediate postoperative bronchoscopic aspiration and x-ray examination of the patient before he leaves the operating table will reduce the incidence of postoperative pulmonary complications.

The figures used in this study were taken from the records of General Hospitals through the courtesy of the following chiefs of Anesthesia Sections: Baxter General Hospital, Major Leonard M. Taylor, Brooke General Hospital, Lieutenant Colonel J. W. Winter, Bruns General Hospital, Captain Carl F. Mast, Fitzsimons General Hospital, Major Bryce Stearns, Kennedy General Hospital, Captain Frank Galiato, Percy Jones General Hospital, Major Edward B. Tuohy, Walter Reed General Hospital, Lieutenant Colonel Harold F. Bishop, and Lieutenant Colonel Lloyd H. Mousel.

REFERENCES

1. Beecher, Henry K.: Some Controversial Matters of Anesthesia for Thoracic Surgery, J. THORACIC SURG. **10**: 202, 1940.
2. Bourne, Wesley, Leigh, Digby M., Inglis, A. Nelson, and Howell, G. Rennie: Spinal Anesthesia for Thoracic Surgery, Anesthesiology **3**: 272-281, 1942.
3. Esten, Benjamin: Anesthesia for Thoracic Surgery, New York State J. Med. **43**: 1980, 1943.
4. Moyer, C. A.: Major Changes in the Fundamental Relationships of the Respiratory Drive Mechanisms During Evipal and Pentothal Anesthesia, With Special Consideration of Possible Applications to Transpleural Surgery, J. THORACIC SURG. **11**: 131, 1941.
5. Neff, William, Phillips, Wilson, and Gunn, Grace: Anesthesia for Pneumonectomy in Man, Anesthesiology **3**: 314-322, 1942.
6. Nosworthy, M. D.: Anaesthesia in Chest Surgery, With Special Reference to Controlled Respiration and Cyclopropane, Proc. Roy. Soc. Med. **34**: 479-506, 1941.
7. Phillips, Francis, Livingstone, H. M., and Adams, W. E.: A Clinical Consideration of Anesthesia in Intrathoracic Operations, Anesth. & Analg. **20**: 78-87, 1941.
8. Phillips, Francis J., Livingstone, H., and Engel, R.: Anesthetic Results in Over 500 Thoracic Surgery Operations, Anesth. & Analg. **19**: 11-18, 1940.
9. Randolph, Howell S., and Kober, Leslie, R.: The Use of Pentothal Sodium Anesthesia in Thoracic Surgery, J. A. M. A. **121**: 1215-1217, 1943.
10. Wiggin, Sidney Cushing, and Schultz, Philip E.: Anesthetic Procedures in Thoracic Surgery, Am. J. Surg. **54**: 4-17, 1941.